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SURGERY

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SURGERY

VOL. 35 APRIL, 1954 No. 4

Original Communications

TRANSPARIETAL SPLENOPORTAL ROENTGENOGRAPHY AND RESEARCH ON PORTAL HYPERTENSION

OUR CLINICAL EXPERIENCE

A. M. DOGLIOTTI, M.D.,* AND S. ABEATICI, M.D.,** TURIN, ITALY

PORTAL hypertension is the common denominator of several morbid processes, which differ from each other as to their site, etiology, and pathogenesis, although all are prone to cause some circulatory interference with the intrahepatic or extrahepatic portal vein or with any one of its roots. Therefore, the picture of portal hypertension does not form a well-defined nosologic unit, being only the symptomatic expression of a hemodynamic disorder consequent to the established venous obstruction. The pathoanatomic variety of all obstructive factors is reflected by a range of clinical features, all having the common background of portal stasis, but in varying degree, depending on the site, nature, and extension of the obstructive process and the capacity of a compensatory circulation. Thus one can see how serious cases, characterized by such dramatic features as digestive hemorrhage with splenomegaly and clear subcutaneous venous network, might fade away, through several steps, toward the latent or initial forms wherein a persistent meteorism or a moderate splenic tumor are the only revealing signs. Only with the aid of the diagnostic means we now have can we locate, with sufficient accuracy, the site of the portal lesion and appraise the degree of the circulatory alteration, even in those cases which are clinically silent, atypical, or monosymptomatic. It is generally agreed that a classification of the causes of the portal block should be worked out upon the basis of topographic principles; this seems to be justified to some extent by the variety of pathogenic, clinical, and therapeutic features. Thus, we have two major groups of obstructive factors: extrahepatic and intrahepatic. A more precise differentiation is given by pathoanatomic considerations, which allow us to divide the causes of the portal block according to the classification in Table I.

A morphologic study of all these obstructive factors and a sound evaluation of the consequent circulatory disorders can be safely carried out through a preoperative phleboroentgenographic examination of the portal system; this we

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usually do following the method of "transparietal splenoportography," which was conceived and worked out in our School (Abeatici and Campi), and which is now commonly performed.

TABLE I

1. *Extrahepatic obstructive factors*
   - (a) Congenital lesions: Stenosis; Angiomatosis of the smaller omentum; Cruveilhier-Baumgarten syndrome
   - (b) Thrombosis
   - (c) Compressions (by): Inflammatory processes (Acute; Chronic); Benignant tumors (Primary; Secondary); Malignant tumors (Primary; Secondary)
2. *Intrahepatic obstructive factors*
   - (a) Congenital lesions
   - (b) Infiltrations
   - (c) Parenchymatous hepatitis: Acute; Subacute; Chronic
   - (d) Biliary lesions (cholestatic fibrosis)
   - (e) Circulatory lesions (hepatic stasis)
   - (f) Focal lesions: Inflammatory; Parasitic
   - (g) Neoplasms: Primary; Secondary

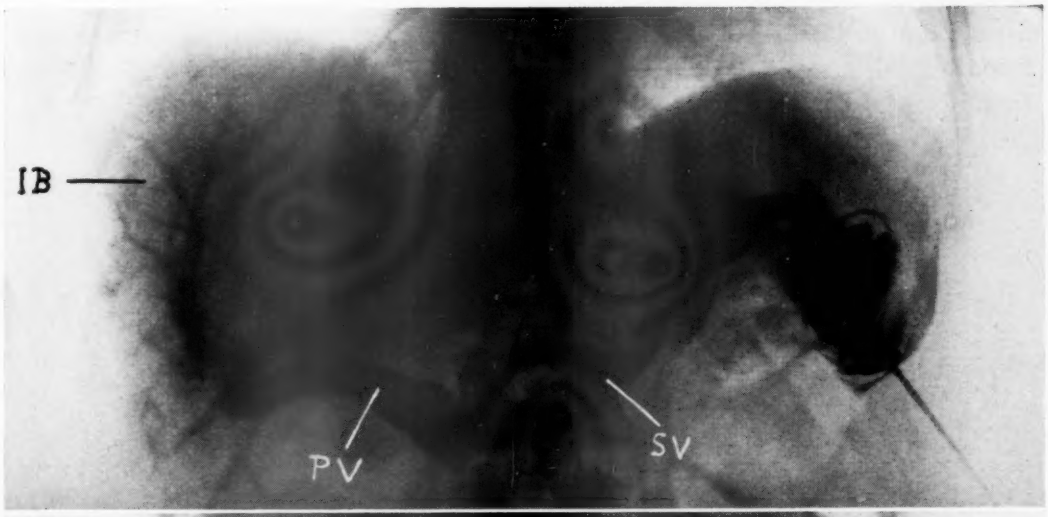
Technique for Transparietal Splenoportography.—This technique is based on visualization of the portal system by means of a percutaneous injection of a radiopaque preparation into the splenic parenchyma. Experimental research, trials on corpses, and clinical experiences enabled us to establish some technical details which make this type of examination easier and quicker.

The splenic area being delimitated by percussion, we locate the ninth or tenth intercostal space; here, on the middle axillary line generally, we give a local novocaine anesthesia including the skin and underlying tissues. Then we perform the splenic puncture employing a needle 12 cm. (five inches) in length and 1.5 mm. (one-sixteenth of an inch) external gauge. The needle, having entered the peritoneal cavity, must be directed upward medially and backward; after a few centimeters we feel a soft elastic resistance, beyond which we continue further for from 4 to 5 cm. (about two inches). At this point, the mandrin being withdrawn from the needle, the dripping of the blood assures us of the right position. The radiopaque preparation, a 70 per cent solution of Joduron, may then be injected with a common 50 c.c. syringe; the quantity injected varies from 15 c.c. to 40 c.c. The injection must be performed very quickly and should never last more than three to four seconds; it is easily performed without any resistance. The introduction of the liquid is practically painless, so that we have abandoned general anesthesia, which we used in earlier cases (Fig. 1).

Also in order to get a functional evaluation of the portal system, we must have serial roentgenograms made according to the following chronological classification: One, two, three, five, eight, and eleven seconds after the beginning of the injection. The hemodynamic conditions of the splenoportal circulus can

thus be determined with sufficient accuracy, since we have a graphic survey of changes of the opacifying time in different segments of the venous branching, and we are able to determine actual diffusion curves.

Fig. 1.



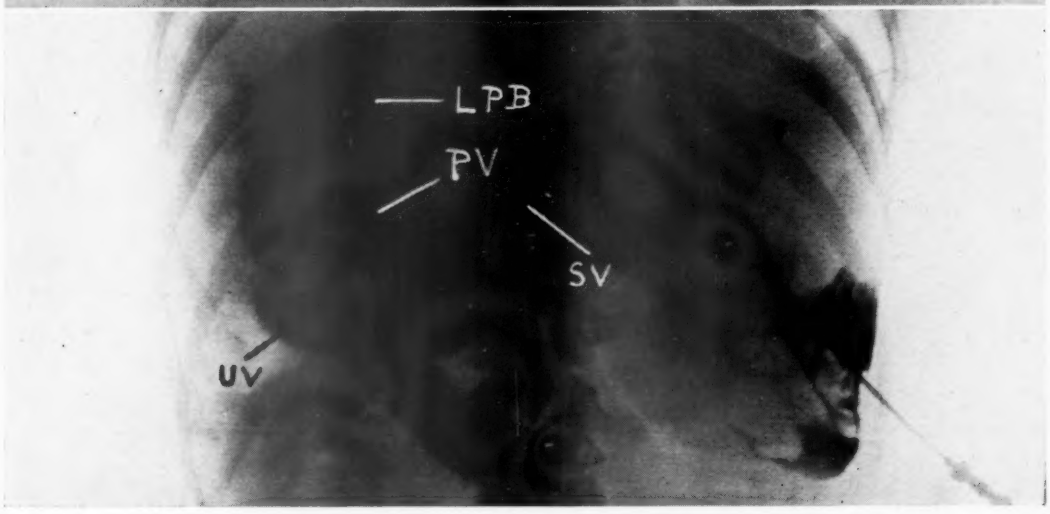


Fig. 2.

Fig. 1.—Normal splenoportal roentgenography. *SV*, Splenic vein; *PV*, portal vein; *IB*, intrahepatic branches.

Fig. 2.—Cruveilhier-Baumgarten syndrome. *SV*, Splenic vein; *PV*, portal vein; *LPB*, left portal branch; *UV*, umbilical vein.

Considerations of Some Cases of Portal Hypertension.—Both clinical and phleboroentgenographic examinations made in twenty-one cases of portal stasis (1952 to 1953) have given us new evidences of the multitude of obstructive factors and of the variety of nosologic features which seem to be bound to the nature of the morbid process, to the site of the portal block, and to the capacity of collateral circulation. The etiological features, which we happened to recog-

nize in our patients, are thus far from constant, and not at all alike in all cases. Ascitic liquid, for instance, was present in twelve cases, and it is not easy to determine its origin. The supposition, put forward by Caroli, Paraf, and Schwarzmann, that the presence of ascitic liquid might be a consequence of insufficient natural portacaval connections seems to be rather fascinating, and sustained by findings on corpses; even our portographic researches seem to add more value to it; however, we think it needs a deeper study and further confirmation. We must bear in mind the parts played in the pathogenesis of the abdominal effusion by both hepatargy and protein unbalance.

Fig. 3.

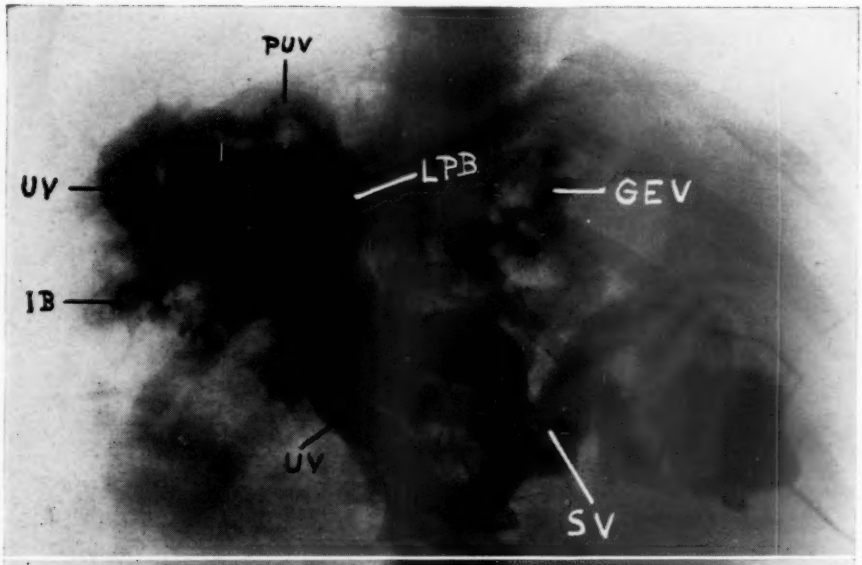


Fig. 4.

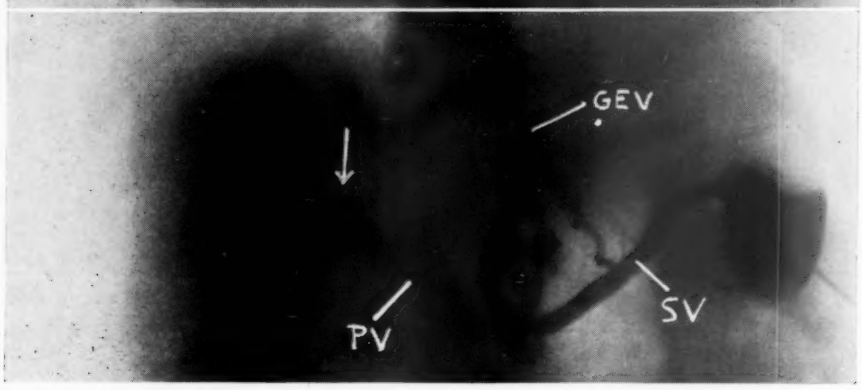


Fig. 3.—Cruveilhier-Baumgarten syndrome. *SV*, Splenic vein; *GEV*, gastroesophageal veins; *LPB*, left portal branch; *UV*, umbilical vein; *PUV*, paraumbilical vein; *IB*, intrahepatic branches.

Fig. 4.—Thrombosis of the left portal branch. *SV*, Splenic vein; *GEV*, gastroesophageal veins; PV, portal vein.

Gastroenteric hemorrhage, which is by far the most dramatic feature of portal hypertension, was seen in five cases of extrahepatic obstruction and in one case of intrahepatic obstruction. The pathogenesis of this type of hemor-

rhage, either in the form of hematemesis or in the form of melena, is normally ascribed to the breaking off of gastroesophageal phlebectasia. Notwithstanding the importance of portal stasis, the vascular fragility should never be underestimated nor should the concomitant alterations regarding prothrombinemia and the hematic proteins.

Fig. 5.

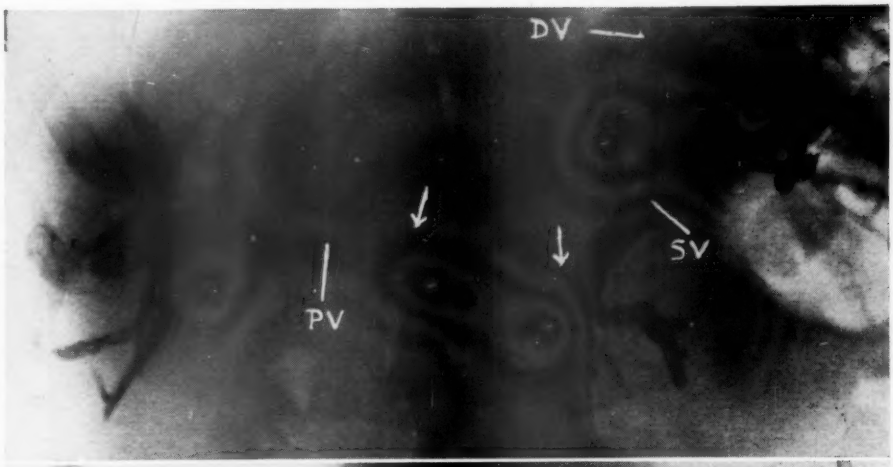


Fig. 6.

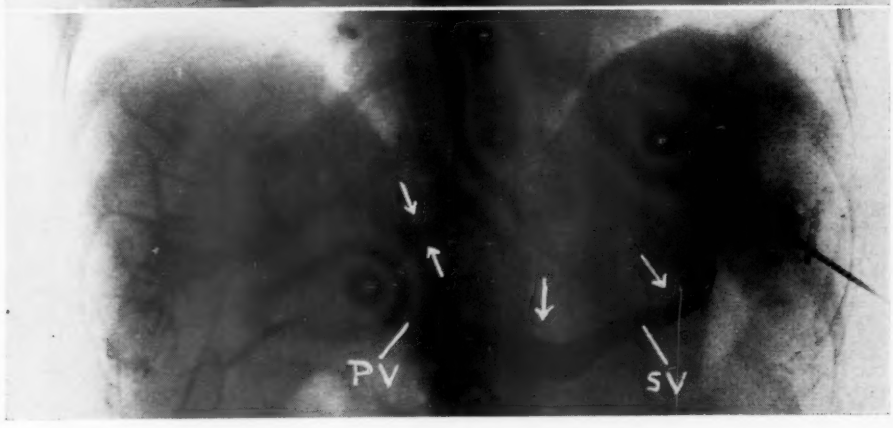


Fig. 5.—Pancreatic carcinoma. Compression of splenic vein. *DV*, Diaphragmatic veins; *SV*, splenic vein; *PV*, portal vein.

Fig. 6.—Pancreatic pseudocyst. Displacement of the splenic vein, compression of the left portal branch. *SV*, Splenic vein; *PV*, portal vein.

Another interesting feature of portal hypertension lies in the lienal behavior. We noticed that the size of this organ is likely to change widely from one case to the other, so that we had forms with a clear splenomegaly while in many other instances the size of the spleen was virtually normal or only slightly above average. This varying behavior of the spleen may be related to the greater or lesser availability of the compensatory collateral circulation, the latter depending on the site of the portal obstruction.

The multitude of factors involved in portal hypertension and the many individual variations of venous stasis are both directing the choice for surgical

treatment toward eclecticism. The ideal therapeutic action should be represented by the complete removal of the venous obstruction. However, this can be done quite rarely, only in a few forms with extrahepatic compression or with suprahepatic stasis. More frequently, the surgical therapy must be directed only toward mitigating the existing hypertension either in the whole portal area or in a part of it. Such a palliative aim can be reached through a series of surgical interventions, ranging from simple splenectomy to the various types of portacaval venous anastomoses.

Fig. 7.

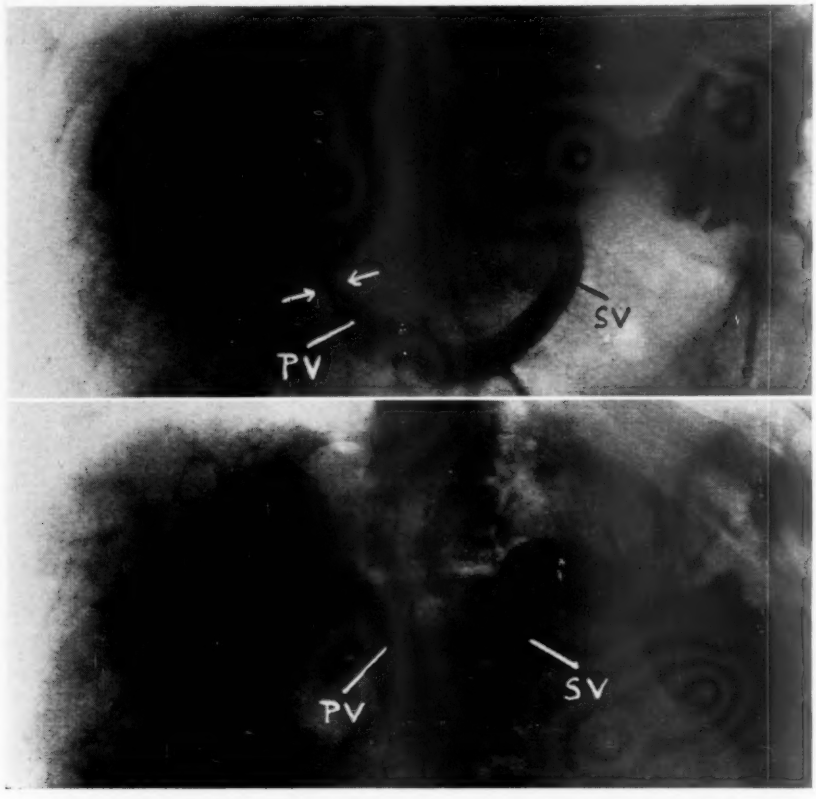


Fig. 8.

Fig. 7.—Lymphadenal metastasis of the hepatic hilus from ovarian carcinoma. Ring compression of the portal vein. *SV*, Splenic vein; *PV*, portal vein.

Fig. 8.—Hepatic fibrosis in multilobular liver. Reduction of the intrahepatic branching, missing opacification of the left lobe, displacement of the very short left portal branch. *SV*, Splenic vein; *PV*, portal vein.

Splenectomy, considered a minor therapeutic intervention in the treatment of portal stasis, is clearly advisable in cases where an obstruction can be found before the confluence of the lienal vein with the coronary vein (vena coronaria ventriculi); these are cases where hypertension is confined to a short portion of the lienal vein, so that it is clearly unnecessary to perform a shunt afterward.

A noticeable reduction of blood supply within the portal area can also be obtained by means of splenic artery ligature, thus producing a fall of one-third

of the whole stream. Besides, the stagnant blood from the portal area is likely to flow back through the lienal veins which are left undamaged and to reach some collateral way through the already existing anastomosis. Ligature of the splenic artery is particularly recommended for depauperated patients who are bodily unable to suffer surgical interventions of greater importance; moreover, it is recommended in patients with congestive splenopathy and high pressure in the portal area where, for some reason or another, it is not possible to perform normal splenectomy and portacaval shunting.

Fig. 9.

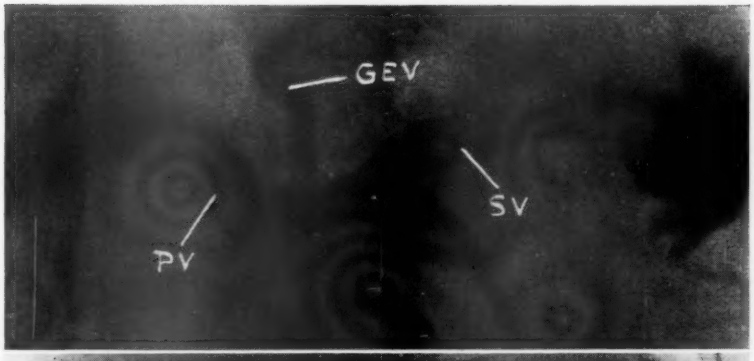


Fig. 10.

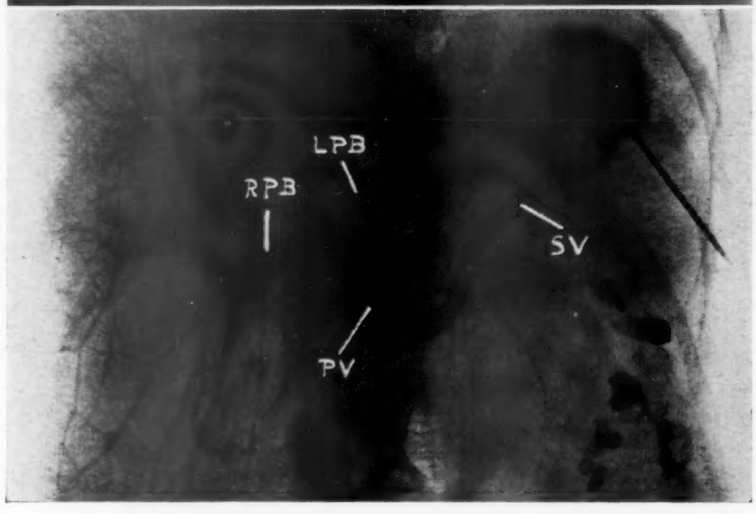


Fig. 9.—Hepatic fibrosis in multilobular liver. Splenoportal roentgenography three months later. *SV*, Splenic vein; *GEV*, gastroesophageal veins; *PV*, portal vein.

Fig. 10.—Hepatic steatosis: hepatomegalia, thinned intrahepatic branches. *SV*, Splenic vein; *PV*, portal vein; *RPB*, right portal branch; *LPB*, left portal branch.

Among the several surgical interventions devised to relieve portal stasis by creating new ways for the blood to discharge, portacaval anastomosis (and its variant, splenorenal anastomosis) offers the best therapeutic possibilities. Portacaval anastomosis produces an effective and long-lasting palliative action, especially in those cases where all important disturbances are related to the portal hypertension. This venous shunting is then likely to establish a wide drain

to the flowing down of the stagnant blood, and the implied amendment to the circulation removes the serious danger of gastroesophageal hemorrhage which has, in these cases, a purely mechanical origin.

Indeed, our most satisfactory result was obtained by splenorenal shunt in a case of Cruveilhier-Baumgarten syndrome with repeated massive hemorrhages from esophageal varices and developed periumbilical venous network (Fig. 3). The patient had significant relief, and the lowering of the portal hypertension was evidenced by the stopping of the gastroesophageal hemorrhages and by the disappearance of the abdominal veins.

Fig. 11.

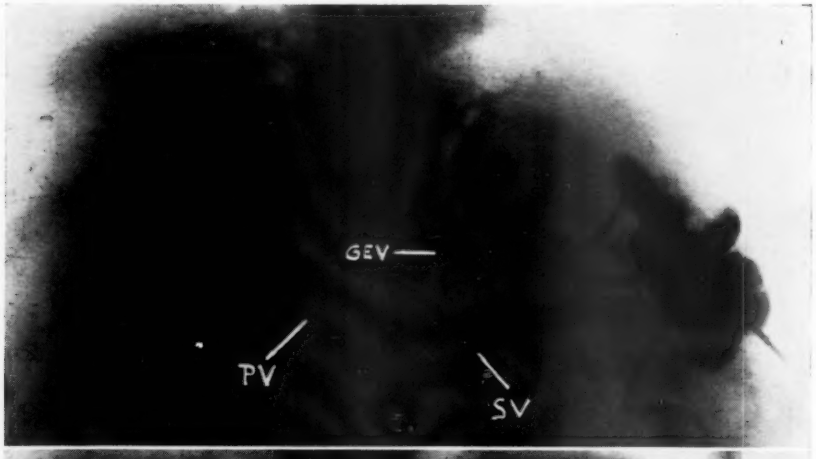


Fig. 12.

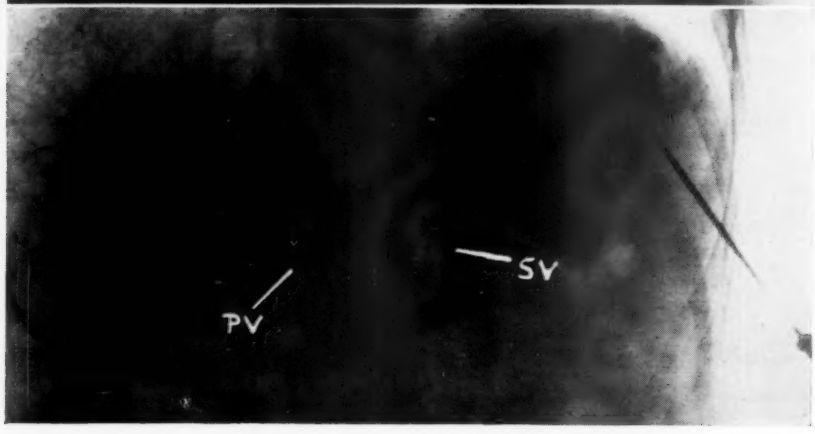


Fig. 11.—Atrophic cirrhosis: strong reduction and thinning of the intrahepatic branches. *SV*, Splenic vein; *GEV*, gastroesophageal veins; *PV*, portal vein.

Fig. 12.—Cholestatic fibrosis: hepatomegalia, reduction and thinning of the secondary intrahepatic branches. *SV*, Splenic vein; *PV*, portal vein.

Portacaval anastomosis is not to be recommended, on the contrary, in cases of intrahepatic obstruction and in cases of cirrhosis of the liver, where portal hypertension is a second-rate feature, the most important disturbances being related to the liver involvement, and the circulatory alterations being far more

complex. Other interventions have been suggested for the treatment of cirrhosis; among them is ligature of the hepatic artery, founded on the assumption, merely theoretical, of an overturn of relationships between arterial circulation and portal circulation within the course of the pathologic process. Ligature of the hepatic artery would produce a reduction of the arterial pressure within the intrahepatic arterial branching, thus making easier the portal reflux. Besides, the ligature, being made at the origin of the hepatic artery, would promote a drop of the portal pressure, especially when associated with the similar ligature of the lienal artery. However, the method of action of the hepatic artery ligature has not yet been ascertained, nor have the theoretical foundations of this intervention been confirmed.

More practical seems to be the arterialization of the portal vein, as suggested by Paterni and as performed by Pettinari and associates, by means of anastomosis between the splenic artery and vein or between the splenic artery and portal vein. The arterial blood flowing in through the whole portal area produces an increase of the venous circulation, thus improving the oxygenation of the hepatic parenchyma; experimental data and early clinical results seem to support this possible way of improving the circulatory conditions of a diseased liver.

CONCLUSIONS

As a conclusion, we believe we can safely state that the surgical treatment of portal hypertension, being subordinate to the characteristics of the primary lesion and to the importance of circulatory stasis, always requires a thorough preoperative study of the circulatory conditions and a careful examination of the morphologic features of the venous branching in this area. A vague diagnosis of hypertension is not sufficient as a rule, the diverse nature of the morbid process and the different sites of the consequent obstruction giving way to several surgical problems. To the solution of these problems, transparietal portal roentgenography adds, in our opinion, an important and definite contribution. It enables the surgeon to determine, prior to intervention, the characteristics of the primary lesion, the importance of the hemodynamic disorder, and the possibilities for a compensatory circulation to the portal one. Therefore, we hope that this procedure may gain a wider clinical application.

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LYMPH NODE METASTASES: EXPERIENCE WITH AORTIC LIGATION OF INFERIOR MESENTERY ARTERY IN CANCER OF THE RECTUM

JACK W. MCELWAIN, M.S., M.D.,* HARRY E. BACON, M.D., AND HOWARD D. TRIMPI, M.D., PHILADELPHIA, PA.

(From the Department of Proctology of Temple University Medical School)

INTRODUCTION

SINCE Reybard[68] performed the first resection and anastomosis for cancer of the large bowel in 1832, surgeons have been striving to extend the scope of operations to combat this regrettable condition. With the ever-increasing knowledge of anesthesia, blood replacement, and sepsis control, more radical surgery is becoming possible. In order to utilize most effectively these recent advances in regard to the treatment of large bowel malignancy, certain anatomic and pathologic limitations must be understood.

Because extended surgical procedures for cancer of the colon, rectum, and anus are instituted in an effort to remove the dispersion routes of malignant cells as well as to extirpate the local growth, it is important for the colonic surgeon to know fully the methods and pathways of tumor dissemination. One of the most important routes of cancer spread is via the lymphatic system. Indeed, Moynihan[57] in 1908 stated that "the surgery of malignant disease is not the surgery of organs, it is the anatomy of the lymphatic system." There has been some monumental work on the lymphatic system in recent years, especially in regard to cancer of the distal colon and rectum. Most of these studies, however, have only embraced that section of the lymphatic pattern distal to the left colic branch of the inferior mesenteric artery.

Extended surgical procedures on the colon, rectum, and anus frequently involve ligation of large supplying vessels. There is little disagreement as to the safety of this course of action when large branches of the superior mesenteric artery are ligated, but some controversy still exists regarding the advisability of ligating the inferior mesenteric artery above its left colic branch when an attempt is being made to preserve the blood supply to the distal large bowel. Recent work by Ault[3] has stimulated renewed interest in this subject.

The purpose of this paper is to report the results found in the clearing of intramesenteric lymph nodes from 90 cases of cancer of the colon, rectum, and anus in which a ligation of the inferior mesenteric artery was performed at its aortic origin. No attempt has been made to study the extramesenteric lymph nodes, although a discussion of their importance will be made.

Received for publication, Aug. 3, 1953.

*Thesis submitted in partial fulfillment of requirements for the degree of M.S. in Proctology.

ARTERIAL BLOOD SUPPLY

The blood supply to the colon and rectum has been well demonstrated by many authors.[2, 22, 35, 38, 76] The left half of the transverse colon, the descending and sigmoid colons, and the upper rectum are supplied by the inferior mesenteric artery. It arises from the anterior surface of the aorta 3 to 4 cm. above the junction of the common iliac arteries. This is usually about 4 cm. below the duodenum, but in rare instances the origin may be directly behind that organ. As it crosses the left common iliac artery and continues into the pelvis, it is renamed the superior hemorrhoidal artery.

The first branch of the inferior mesenteric artery is the left colic, which originates 2 to 4 cm. from the aorta and courses beneath the peritoneum. Arising from the inferior mesenteric artery below the left colic are the sigmoidal branches. These vary from two to four in number and run beneath the peritoneum to supply the lower ascending and sigmoid colons. The superior hemorrhoidal artery divides into two branches at the third piece of the sacrum. These in turn redivide to supply the rectum.

Of particular interest to the surgeon performing a ligation of the inferior mesenteric artery at its aortic origin is the anastomotic potential of the marginal artery. This artery originates in the cecal arcades and courses along the entire large bowel to end in the sigmoidal arcades. It is located 1 to 8 cm. from the bowel wall, being somewhat nearer to it from the transverse colon to the rectum. Frequently it forms secondary arcades, but rarely tertiary. The only site where this artery may be inconstant is along the ascending colon where, in 5 per cent of cases, numerous separate branches terminate in the bowel.

Its function as a collateral blood channel between the two sides of the colon was questioned by Litten in 1875, who found that cutting the superior mesenteric artery in dogs led to gangrene due to poor anastomosis with the inferior mesenteric. In 1893, Morestin (as quoted by Archibald) ligated the inferior mesenteric artery without causing gangrene. This work was substantiated by Archibald,[2] who discovered that material could be injected into the superior mesenteric artery of cadavers and then be found in the superior hemorrhoidal vessels despite the ligation of all the branches of the inferior mesenteric artery some distance from the bowel. In 1907, Sudek,[77] being annoyed at the frequent failure of distal blood supply following perineal resections of the rectum, studied the various colonic anastomotic channels by injections and roentgenography and then defined his well-known "critical point." Sudek claimed that ligation of the superior hemorrhoidal artery distal to the last sigmoidal branch would not permit dye injected into the inferior mesenteric artery to flow into the upper rectal blood vessels. His original studies were not made in reference to the Miles procedure or to end-to-end resections. He concluded that perineal resections of the rectum should be supplemented by transabdominal ligation of the superior hemorrhoidal artery proximal to the last sigmoidal branch, which would have the added benefit of permitting more adequate mobilization of the bowel. This work was confirmed by Hartmann[44]

in 1909. However, he placed the level of the ligation at the sacral promontory. In 1910, Rubesch,[70] while studying gangrene of the rectum after operations, stressed the importance of this artery near the bowel. In 1913, Drummond[22] ligated all the main arteries to the colon and reported that material injected into the ileocolic artery entered the sigmoidal vessels without interruption. It was he who most accurately described the location and course of the marginal artery which now rightfully bears his name.

Other authors have added a word of caution, however, about the indiscriminate ligation of large colic vessels. Manasse[48] felt that the marginal artery, although present in the sigmoid area, was weak, and communicated poorly with the last sigmoidal branch. Pope and Buie[63] have shown a varying pattern in the pelvic colon vessels, and pointed out the frequent paucity of anastomosis with the marginal artery. Desmarest[20] and Jamieson and Dobson[45] do not advocate the generalization that the marginal artery is infallible. Steward and Rankin[76] point out that care must be taken not to draw too many conclusions from cadaver studies alone, as the smooth muscle of fixed vessel walls often contracts. Others who rely moderately on the anastomotic function of the marginal artery are Pope and Judd,[64] Sunderland,[79] Bacon and Smith,[9] and Muir.[58]

LYMPHATIC DRAINAGE

The lymphatic drainage system of the large intestine originates in the mucosa, where tiny, blind-end lymph capillaries begin in the superficial epithelium. These pathways anastomose to form a subepithelial plexus, which in turn joins the more coarse tubules of the submucosa. Some of the primary lymphatics contain smooth muscle fibers which contract and milk the lymph toward the collecting channels. From the submucosa, the lymphatics course in a radial direction through the muscle coats to ramify in a subserous plexus. A few channels run for a short distance longitudinally between the circular and longitudinal muscle coats, but for the most part the initial direction of flow is in a radial direction. This is an important concept in approaching the problem of intramural spread of tumor cells. The flow of lymph is aided also by the presence of intermittent constrictions in the lymph channels which correspond to the valves of the venous system. Located in the subserous plexus of lymphatics are small lymph follicle aggregations called epicolic nodes by Jamieson and Dobson.[45] The lymph stream filters through these nodes and collects into larger channels which course into the para-colic nodes located about 1 cm. from the bowel wall. As the lymphatics embryologically bud from veins, it is not difficult to understand why the course of the lymphatic system parallels that of the vascular for the most part. From the paracolic glands, efferent lymph follows along ever-enlarging pathways to the intermediate nodes. These are fewer in number, and located at the branches of the large arteries such as the colic and superior hemorrhoidal vessels. Principal nodes are a fourth line of filtration found at the origin of the main large bowel arteries, such as the superior and inferior mesenteries. As a rule, the foregoing is the usual route taken by lymph. However, as reported

by Rouvière[69] and more recently by State,[75] there may be skip patterns of drainage. Rouvière demonstrated that pathways from the hepatic flexure and especially the sigmoid colon may drain directly to the intermediate or principal nodes. Jamieson and Dobson[45] stated, however, that the paracolic nodes in the distal two-thirds of the transverse colon and the splenic flexure are never by-passed. When lymphatic blockage occurs because of tumor metastases, the lymphatic spread is from paracolic to paracolic nodes.

Colon.—The ileocecal region is rich in lymphatics. Many paracolic and intermediate nodes are also in existence, with large principal nodes occurring at the origin of the ileocecal artery. The ascending colon is less rich, but intermediate nodes can be demonstrated along the ascending and descending branches of the right colic artery. A principal node is present at the superior mesenteric angle. The transverse colon and the flexures are drained through several paracolic and intermediate nodes with large principal aggregations at the middle colic origin. The descending colon is poorly endowed with nodes except for a few paracolics and one or two intermediates. The sigmoid colon, however, subtends many lymph nodes. Epicolic lymph follicles are found in abundance in the appendices epiploicae. Large principal nodes exist at the origin of the inferior mesenteric and left colic vessels. Grinnell[42] has discovered as many as ten nodes in this angle, which has been called by some the "axilla of the abdomen."

Rectum.—The lymphatic anatomy of the rectum and anus does not follow completely the vascular pattern, and although many research workers have written extensively on the subject, some confusion still exists. There are three pedicles of spread as clarified by Sauer and Bacon[71]: superior, lateral, and inferior.

Superior pedicle: This pedicle contains more lymphatics than the other two and is the main drainage system of the rectum. The entire rectum and the anal canal are drained by this pedicle, which follows the distribution of the inferior mesenteric artery in the mesocolon. It is a constant system, for dye injected anywhere in the rectal or anal canal mucosa can be demonstrated in inferior mesenteric lymph nodes. Channels from the anus and rectum pass through the pararectal nodes of Gerota, which are from four to ten in number, and located above the levator muscles on the posterolateral rectal wall, to the intermediate nodes about the superior hemorrhoidal bifurcation. One large node situated directly in the angle of the bifurcation receives nearly all the lymphatic channels and, consequently, has been named the "principal node of the rectum." Effects from there travel along the superior hemorrhoidal artery to reach the principal nodes at the origin of the inferior mesenteric artery. These nodes are from five to ten in number, and lie in the superior angle to the left of the aorta. A few tracts follow the inferior mesenteric vein to the pancreaticoduodenal nodes higher in the abdomen. Rouvière[69] stated that a few lymphatic pathways from the low rectum may by-pass the pararectal nodes to enter the intermediate nodes, but that only a rare pathway will be found to extend directly from the rectum to the inferior mesenteric nodes. This was also noted by Villemin.[81]

Lateral pedicle: This pedicle, often called the middle, consists of four drainage patterns: the middle hemorrhoidal, the lateral sacral, the anterior, and the middle sacral.

The most important of these is the middle hemorrhoidal, which consists of paired groups of channels draining the distal 4 cm. of the rectum. These lymphatics rarely extend into the anal canal. They gather in one or two lymph nodes situated in the lateral rectal ligaments. These nodes may be located directly on the bowel wall or 1 to 2 cm. laterally. Efferents course laterally and cephalad in these ligaments beneath the superior wing of the endopelvic fascia to nodes along the internal iliac artery. An inconstant obturator lymph node may receive some channels. A few pathways may extend directly from the rectum to the iliac nodes. Proximal drainage then enters the nodes on either side of the aorta.

The second group of lateral pathways of spread is along the lateral sacral vessels. Lymphatics from the coccygeal area, anastomosing with those of the middle sacral, drain the distal 4 cm. of rectum and anal canal. They follow the anterior branches of the paired lateral sacral vessels along the hollow of the sacrum beneath the inferior wing of the endopelvic fascia to the internal iliac nodes and thence to the aorta. On occasion, large nodes may be found just distal and lateral to the promontory of the sacrum, receiving many of these channels.

A third group of channels classified as lateral spread is the anterior. Reinhold[67] in his thesis on pelvic lymphatics has described paired tracts draining the distal few centimeters of rectum which arch anteriorly in the layers of rectogenital septum ascending behind the rectourethralis muscle of Roux in the male and the rectovaginal septum in the female. The tracts course laterally over the upper portion of the rectogenital septum toward the internal iliac vessels, anastomosing in some instances with the middle hemorrhoidal lymphatics. The lower vaginal and prostatic lymphatics also may be joined by small numbers of anterior coursing lymphatics, according to Nesselrod.[59]

The fourth group of lymphatic channels composing the lateral mode of drainage is the middle sacral. These channels from the posterior 4 cm. of the rectum and anterior coccygeal area follow the course of the middle sacral artery to the aorta. One or two intercepting nodes are situated just below the sacral promontory.

There is no lateral lymphatic drainage demonstrable higher than 4 cm. above the anorectal line. This level corresponds to the usual location of the middle valve of Houston, 7 cm. from the anal verge. Early workers have called it the "plica transversalis of Kohlrausch," as related by De Oliveira.[19] The absence of lateral spread is abrupt at that level, as demonstrated by a failure of dye to appear in the lateral zones of spread when injection has been made just above. This level of the rectum, therefore, becomes surgically important in the treatment of rectal malignancies.

Inferior pedicle: The columns of Morgagni, the anal canal, and the perianal integument are drained along bilateral lymph channels which follow the course of the inferior hemorrhoidal artery. Pathways extend through the

ischiorectal fossa to the internal iliac and aortic lymph nodes in some instances. A more frequent course of drainage, however, does not follow the vascular supply, but extends beneath the subcutaneous tissue of the buttocks and groin to empty into the superficial and thence the deep inguinal lymph nodes. Most tracts enter the superior and internal group of nodes. These pathways anastomose in the anal canal with the superior hemorrhoidal and to a lesser degree the middle hemorrhoidal lymphatics.

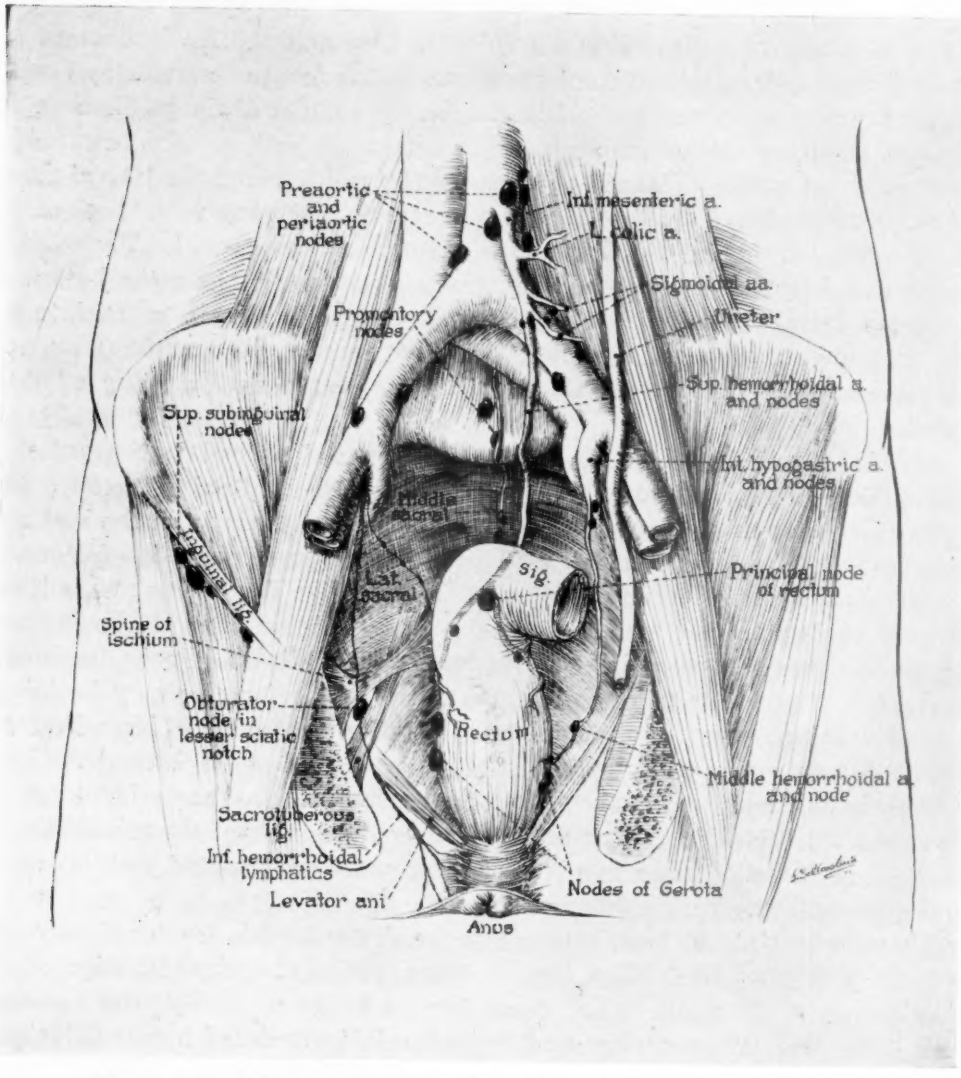


Fig. 1.—Some of the tracts of the lymphatics of the rectum and anus.

Fig. 1 depicts some of the tracts mentioned.

RESEARCH

One hundred fifty patients with carcinoma of the colon, rectum, and anus were subjected to an aortic ligation of the inferior mesenteric artery. Ninety

Fig. 2.

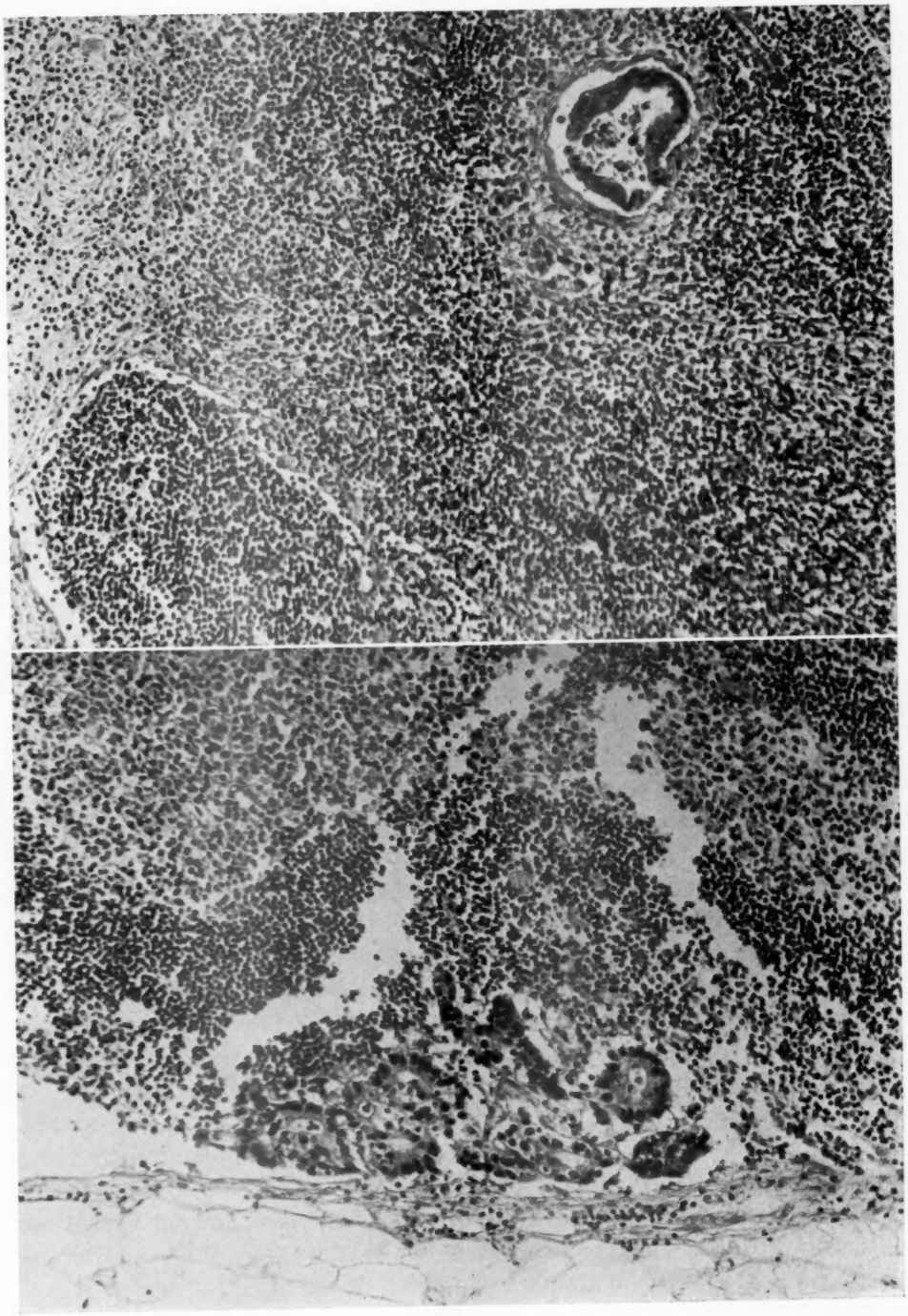


Fig. 3.

Figs. 2 and 3.— Photomicrographs illustrating the appearance of metastases in two nodes.

of the specimens were cleared of lymph nodes by a modified Spalteholz technique[74] with special attention directed toward intermediate and principal node metastases from the variously located lesions. All nodes were sectioned pseudoserially, and questionable areas of metastases were submitted to staff members in the Department of Pathology of the Temple University School of Medicine for consultation. The lymph nodes were removed from the specimens by sharp dissection under transillumination. No attempt was made to study nodes from the lateral routes of spread. Also, no nodes under 2 mm. in diameter were sectioned. Peltier in a recent study[61] on similar material found no metastases in nodes of this size or less, and Grinnell in a personal communication stated that it occurred only in rare instances. Microtome sections were made at 150 micron intervals, and the slides stained with hematoxylin and eosin. No less than three sections of any given mode were made. In some instances, as many as fifteen cuts were made. The average number of fields per node was five to seven.

RESULTS

In all 90 cases, the blood supply to the distal bowel proved adequate despite the ligation of the inferior mesenteric artery at its origin. The only complication encountered was a hematoma in the retroperitoneal space in one instance. Forty-three of the patients were men and forty-seven women. This is in sharp contrast to the usual 3 to 2 ratio of men over women. The average age of the men was 60 years, of the women, 58 years. Of the 90 patients, 54 (60 per cent) evidenced lymph node metastases. Thirty-one of these, or 57.4 per cent, were women, and 23 were men. Eighty-six specimens were of adenocarcinomas, 3 were of squamous cell carcinomas, and 1 was of sarcoma. The last was a malignant mesenchymoma of the distal rectum with 1 regional node metastasis.

Operative procedures instituted included 33 abdominoperineal resections of the rectum with preservation of the sphincters, 31 abdominoperineal excisions of the rectum of the extended Miles type, 25 anterior resections of the bowel with end-to-end anastomosis, and 1 total colectomy. The colectomy was performed on a patient with chronic ulcerative colitis, and an unexpected adenocarcinoma of the sigmoid was discovered. An interesting sidelight was the finding of adenomata in 20 per cent of all the operative specimens. In 3 cases, or 3.3 per cent, a double primary cancer existed. In each case the second tumor was located in the sigmoid colon and was subtended by the same lymphatic drainage pattern as the primary.

The number of lymph nodes dissected from each specimen varied considerably from 4 to 68, with the average being 31 per case. When positive nodes were present, the average number was 33. With negative nodes it was 27. The most nodes positive in a given specimen was 26, the mean being 5.7 per specimen.

Figs. 2 and 3 illustrate the appearance of metastases in two nodes.

Twenty-eight of the specimens with positive nodes contained three or less involved nodes for an incidence of 5.3 per cent. The remaining 26 specimens evidenced metastases in more than three nodes.

The pathologic classification of cancer of the colon and rectum into the A, B, and C groups of Dukes was utilized in this study throughout. Group A encompasses those tumors which are confined to the mucosa and submucosa. Group B includes those tumors which have penetrated into the muscle layer of the bowel wall, but not entirely through it. Group C describes that group of tumors which has invaded to or through the serosal coat. This last group has been subdivided into C_1, which allows lymph node metastases to exist in regional nodes only, and C_2, which includes positive lymph nodes up to the line of mesenteric division. In the 28 specimens which showed three or less positive nodes, 89 per cent were classed as C_1.

Eleven, or 12.2 per cent, of the 90 specimens were removed in the presence of liver metastases. Easily palpable, mesenteric nodes were felt in all these cases but two. Interestingly enough, one specimen with an involved liver had negative lymph nodes upon clearing.

Table I compares the location of the tumors with the type of pathology.

TABLE I

LOCATION	NO.	PER CENT	SQUAMOUS	ADENO-CARCINOMA	SARCOMA
Anus	3	3.3	3		
Low rectum	31	34.4		30	1
Upper rectum	38	42.4		38	
Sigmoid	18	20.1		18	
Total	90	100.0	3	86	1

TABLE II. POSITIVE NODES

LOCATION	A	B	C_1	C_2	TOTAL	
					NUMBER	PER CENT
Low rectum	0	4	6	4	14	46.6
Upper rectum	0	4	13	8	25	65.8
Sigmoid	0	1	9	4	14	70.7
Total	0	9	28	16	53	

TABLE III

LOCATION	NUMBER (GRADE C)	C_1	C_2
Low rectum	14	10	4
Upper rectum	25	17	8
Sigmoid	14	10	4
Total	53	37	16

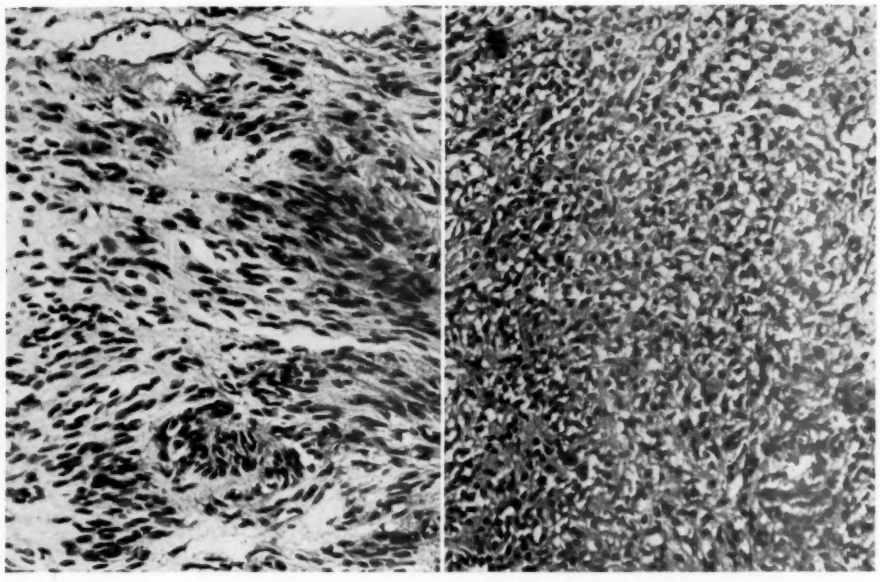
The cases of adenocarcinoma were classified as follows (three squamous cell tumors and one sarcoma were excluded):

	A	*B*	*C*	*Total*
Anus				
Low rectum	2	8	16	26
Upper rectum	3	7	28	38
Sigmoid	1	2	19	22
Total	6	17	63	86

The 54 specimens which contained positive lymph nodes are compared with the grade of tumor in Table II (sarcoma and squamous cell tumors excluded).

Here it may be noted that the 6 tumors of the A group were localized in the bowel and did not metastasize to any lymph nodes. A study of the metastatic pattern of the 9 positive B group tumors revealed only regional node

Fig. 4.—Postoperative specimen in case of E. A., 53-year-old man with malignant mesenchymal tumor involving the rectal wall at 6 cm.



A. *B.*

Fig. 5.—Microscopic appearance of tumor in same case as Fig. 4.

involvement. Thus, in all the cases studied only the C group gave rise to metastases proximal to the intermediate nodes, as may be noted in Table III (sarcoma excluded).

Here it can be noted that 63.6 per cent of all positive nodes from Grade C tumors were regional. Only 16 specimens, or 17.8 per cent of the total 90, evidenced metastatic disease in the principal nodes of the origin of the inferior mesenteric artery. Six of these were from men and 10 from women. The average number of lymph nodes cleared from each of these 16 specimens was 33. The number of positive nodes per specimen was 9.8, or nearly twice as many as in the other positive node cases. All evidenced an orderly pattern of spread through the paracolic and intermediate nodes. One of the high positive nodes from a sigmoid lesion revealed a positive regional, but no intermediate node, and another showed only one positive node directly at the inferior mesenteric root (see Figs. 4 and 5).

Fig. 6.—Postoperative specimen in case of D. E., 65-year-old man with C_2 lesion at 11 cm.

Figs. 4 and 5 illustrate the case of E. A., a 53-year-old man, with a malignant mesenchymal tumor involving the rectal wall at 6 cm.

Table IV reveals the location of the tumor in regard to high positive nodes and after exclusion of the cases with liver metastases.

Therefore, it may be realized that of 90 operative cases, 12 evidenced involved nodes near the origin of the inferior mesenteric artery without liver metastases.

The nodes from 4 of these 12 positive cases feasibly could have been extirpated by ligating the inferior mesenteric artery just distal to the left colic branch. The remaining 8, however, could be adequately removed only by means of a high ligation. Thus, positive nodes would have been left behind in 9 per cent of all the operative cases if a high ligation had not been carried out.

In these 8 cases, 4 evidenced grossly enlarged nodes at surgery, while 4 did not. The average age of these patients was 52 years. Five were women. All 8 primaries were located in the rectum, 5 low and 3 high.

Figs. 6 through 16 illustrate the pattern of spread in the remaining patients with a high number of positive nodes.

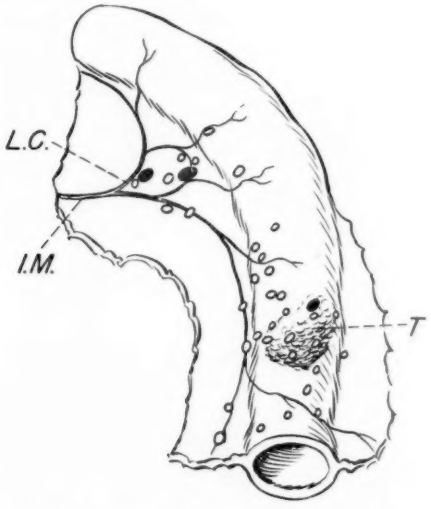


Fig. 7.—Pattern of lymph node spread in same case as Fig. 6.

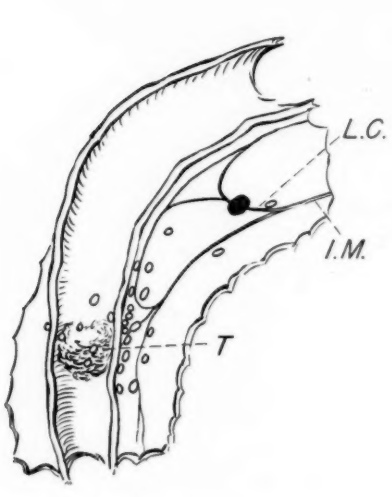


Fig. 8.

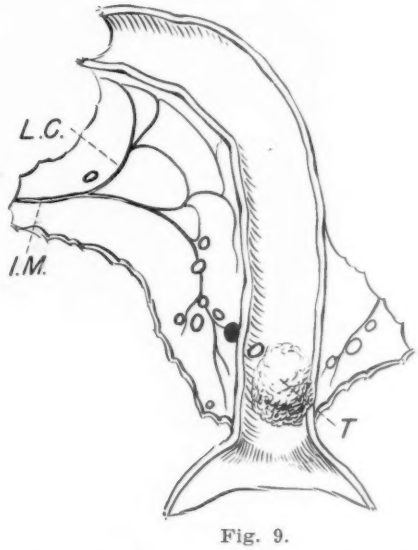


Fig. 9.

Fig. 8.—Pattern of lymph node spread in case of C. McE., 47-year-old man with C_1 lesion at 15 cm.

Fig. 9.—Pattern of lymph node spread in same case as Fig. 8.

The case of D. E., a 65-year-old man with a C_2 lesion at 11 cm., is illustrated in Figs. 6 and 7.

The case of D. McE., a 47-year-old man with a C_1 lesion at 15 cm., is illustrated in Figs. 8 through 10.

Mrs. P. F., a 52-year-old white woman with a type C_2 lesion at 8 cm., underwent abdominoperineal proctosigmoidectomy with preservation of the sphincters (seven nodes positive). (Fig. 11.)

G. A., a 52-year-old white man with a type C_2 lesion at 10 cm., underwent abdominoperineal proctosigmoidectomy with preservation of the sphincters (ten nodes positive). (Fig. 12.)

J. B., a 54-year-old white man with type C_2 lesion at 10 cm., underwent abdominoperineal proctosigmoidectomy with preservation of the sphincters (twenty-six nodes positive). (Fig. 13.)

Mrs. R. S., a 50-year-old white woman with type C_2 lesion at 4 cm., underwent an abdominoperineal excision of the rectum, extended Miles type, plus a panhysterectomy and removal of posterior vaginal wall (seventeen nodes positive). (Fig. 14.)

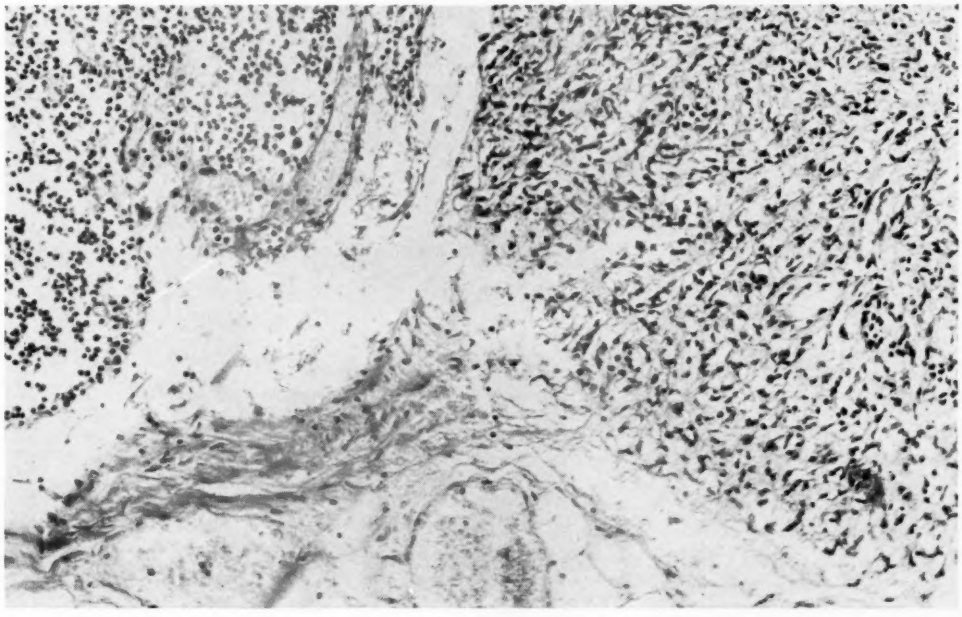


Fig. 10.—Microscopic appearance of the metastasis in same case as Fig 8.

Mrs. M. M., a 63-year-old white woman with a type C_2 lesion at 16 cm., underwent an anterior resection of the sigmoid and rectosigmoid with end-to-end anastomosis (five nodes positive). (Fig. 15.)

Mrs. E. S., a 70-year-old white woman with a type C_2 lesion at 16 cm., underwent an anterior resection of the sigmoid and recotsigmoid with end-to-end anastomosis (five nodes positive). (Fig. 16.)

Table V points out the results of other authors in the over-all clearing of nodes.

Grinnell[42] recently cleared 37 specimens of colonic and rectal cancer removed by high ligations and found 7 instances of positive nodes at the origin

of the inferior mesenteric artery. This represents an incidence of 17 per cent in the present study. Grinnell believed that a high ligation was imperative in all his cases in order to remove these nodes. These findings conform to the

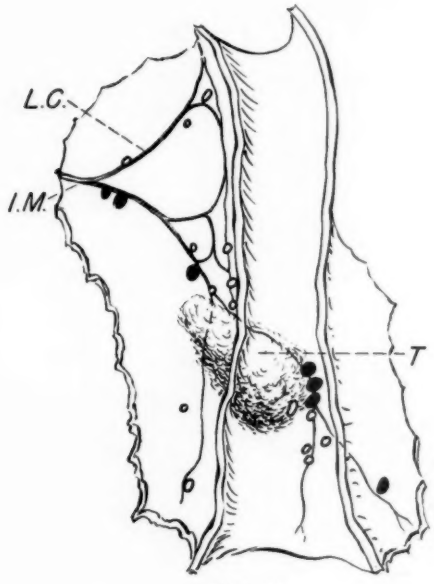


Fig. 11

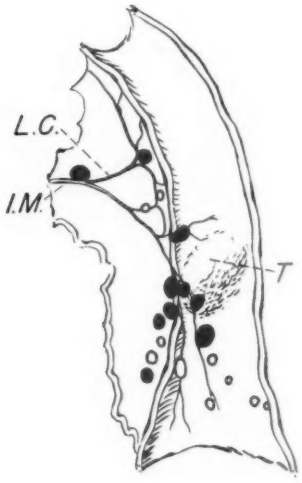


Fig. 12.

Fig. 11.—Pattern of lymph node spread in case of Mrs. P. F., 52-year-old woman with C_2 lesion at 8 cm.

Fig. 12.—Pattern of lymph node spread in case of G. A., 52-year-old man with C_2 lesion at 10 cm.

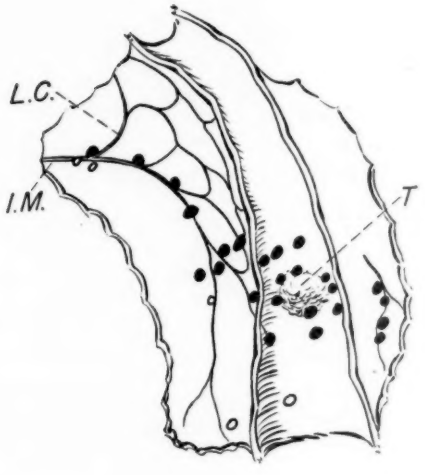


Fig. 13.

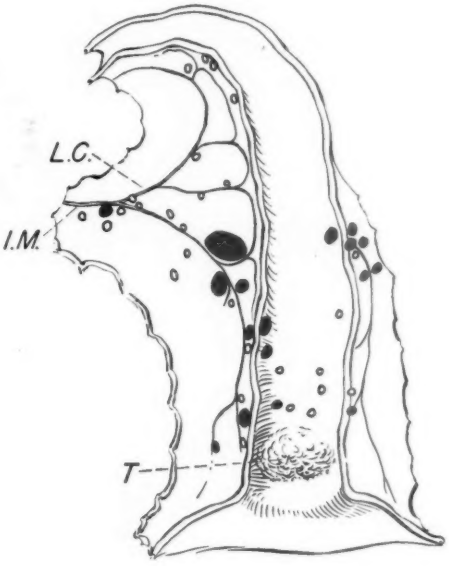


Fig. 14.

Fig. 13.—Pattern of lymph node spread in case of J. B., 54-year-old man with C_2 lesion at 10 cm.

Fig. 14.—Pattern of lymph node spread in case of Mrs. R. S., 50-year-old woman with C_2 lesion at 4 cm.

opinons of Ault,[3] State,[75] and others who recommend the high ligation almost as a routine.

It is interesting to note in this present series that the spread of tumor cells in a superior direction through the lymphatic system from the lower and upper rectum appears to be orderly. No skip areas were demonstrated even to the intermediate nodes. Lesions in the sigmoid colon, however, differ somewhat. Two cases have been demonstrated, one showing a skip of the intermediate nodes and the other of both the intermediate and the regional.

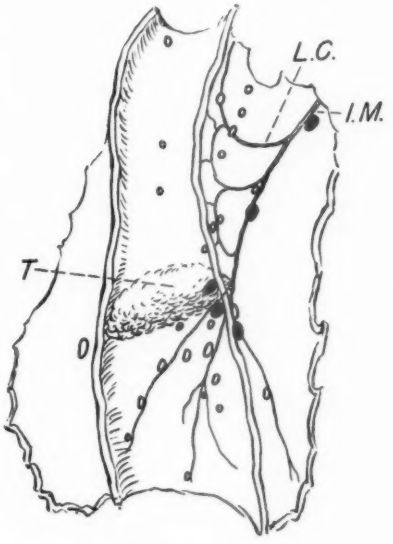


Fig. 15.

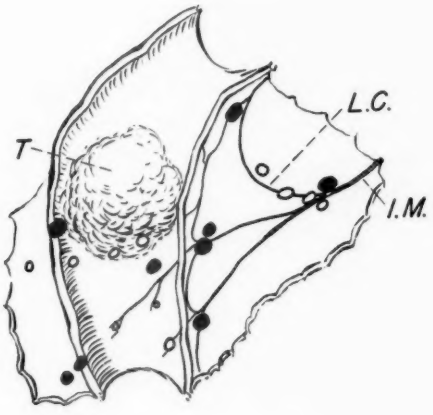


Fig. 16.

Fig. 15.—Pattern of lymph node spread in case of Mrs. M. M., 63-year-old woman with C_2 lesion at 16 cm.

Fig. 16.—Pattern of lymph node spread in case of Mrs. E. S., 70-year-old woman with C_2 lesion at 16 cm.

TABLE IV

LOCATION	POSITIVE HIGH NODES	LIVER CASES EXCLUDED
Anus	0	0
Low rectum	3	3
Upper rectum	8	6
Sigmoid	5	3
Total	16	12

TABLE V

AUTHOR	NUMBER OF SPECIMENS	NUMBER OF NODES	PER CENT POSITIVE
McVay[50]	100	6	47
Wood and Wilkie[87]	100	11	51
Westhues[85]	74	25	59
Gabriel, Dukes, and Bussey[28]	100	28	62
Gilchrist and David[32]	200	52	62.5
Coller, Kay, and MacIntyre[13]	53	67	64
Grinnell[41]	322	38	47
Peltier[61]	25	52	52

Also of interest is the difficult correlation between enlarged lymph nodes at surgery and the possibility of metastases. Gilchrist[33] and Dukes[25] have stated that a 50 per cent error is to be expected. In this series, one-half of the high positive lymph nodes were accompanied by grossly palpable nodes.

SUMMARY

The routes and methods of cancer dissemination in lesions of the colon, rectum, and anus have been discussed, and a review of the vascular and lymphatic supply to the area has been made with special reference to the advisability and practicality of ligating the inferior mesenteric artery at its aortic origin.

Ninety cases of distal bowel resections for cancer with a high ligation of this artery have been presented, and the findings in the cleared specimens reviewed. Sixty per cent of these cases revealed positive lymph nodes, 17.8 per cent of which were located at the origin of the inferior mesenteric artery. Three cases of squamous cell carcinoma of the anus failed to exhibit nodal metastases, but the malignant mesenchymoma of the low rectum did involve a regional node. All the rectal lesions initiated an orderly pattern of lymphatic spread, but the sigmoidal lesions in at least 2 cases revealed a skip pattern. No correlation was attempted between the presence of high positive nodes and lateral lymphatic spread. In at least 8 cases, a ligation of the inferior mesenteric artery below the left colic branch would not have removed positive nodes in the upper portion of the mesentery. Thus, 9 per cent of the operative procedures would have been failures without a high ligation.

CONCLUSIONS

1. Ligation of the inferior mesenteric artery at its aortic origin in the treatment of cancer of the distal colon, rectum, and anus appears to be a safe procedure.

2. The presence of positive inferior mesenteric lymph nodes in cancers of the distal colon, rectum, and anus is frequent.

3. A ligation of the inferior mesenteric artery at its origin should be included in the extirpation of all cancers of the distal colon and rectum.

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AN EXPERIMENTAL STUDY OF THE BUFFERING CAPACITY OF THE CONTENTS OF THE UPPER SMALL BOWEL*

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THE merits of using a short afferent loop in the Billroth II plan of gastric resection have been emphasized.[1-3] It has been shown in this laboratory that the mucosal sensitivity of the small bowel, per se, is not an important factor influencing the increased incidence of stomal ulcers accompanying long afferent loops.[4] It appeared reasonable to explore the thesis that as the length of the afferent loop was increased, the buffering capacity of the small bowel contents was decreased, in other words, that the neutralizing capacity of the alkaline juices decreased progressively as the distance was increased from the pylorus. Cross[5] has shown that in profusing alkaline solutions of known formula, the volume which is returned and the buffering capacity of the solution which is returned are both decreased as the length of the perfused loop is increased.

More exact information regarding the buffering capacity of the contents within the upper small bowel found in the normal animal seemed desirable. A simple, direct approach to the problem was used.

METHODS AND MATERIALS

A series of 32 adult mongrel dogs was used. All animals were being sacrificed incident to other experiments which in no way involved the gastrointestinal tract. The animals were fasted eighteen hours and anesthetized, using 15 mg. of Nembutal intravenously per pound of body weight. A midline laparotomy incision was made. The duodenum and jejunum were isolated and cross-clamped every 10 cm. for 80 cm. The first clamp was placed 3 cm. distal to the pylorus. An intact blood supply was maintained. A clamp also was placed across the hepatoduodenal ligament to prevent continued emptying of bile into the first segment.

Forty cubic centimeters of distilled water was used to lavage each 10 cm. segment. The lavage was performed through the bowel wall using a 15 gauge needle and a 50 c.c. syringe. The lavage solution was injected into and aspirated from each segment five times, over a period of less than one minute. In one-half of the cases, the lavage was begun in the most proximal segment and continued distally. In the remainder, the procedure was reversed. The clamping

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and lavage were carried out as rapidly as possible. The animals were sacrificed at the close of the experiment.

The pH of each specimen then was determined by means of the Beckman Model G pH Electrometer, using glass electrodes. Portions of each specimen were then titrated.

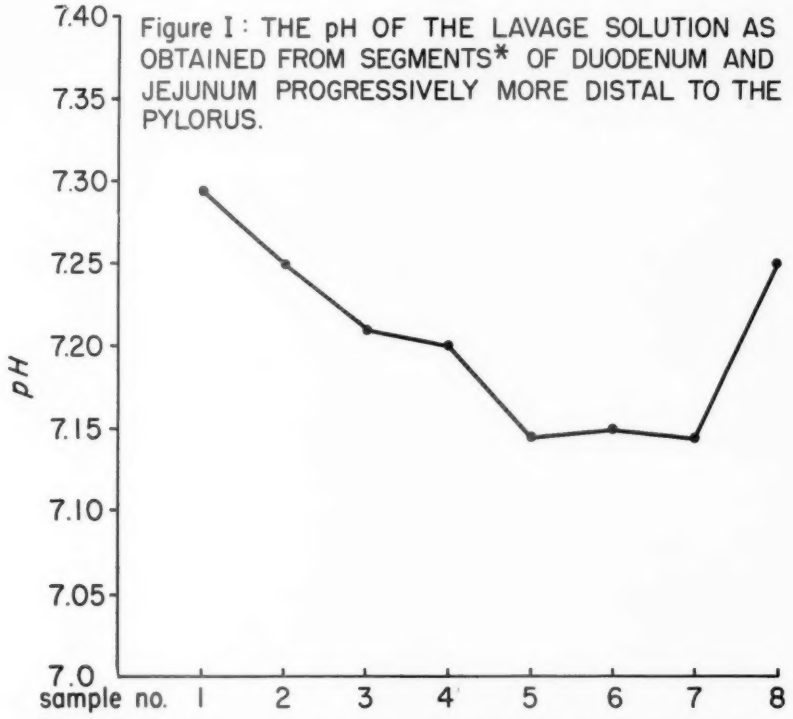

Figure I: THE pH OF THE LAVAGE SOLUTION AS OBTAINED FROM SEGMENTS* OF DUODENUM AND JEJUNUM PROGRESSIVELY MORE DISTAL TO THE PYLORUS.

*Each sample represents a 10 cm. segment of intestine analyzed. Sample no. 1 represents the segment 3 to 13 cm. distal to the pylorus. Sample 8 represents 10 cm. segment at 73 to 83 cm.

Samples from 8 dogs were titrated with 0.01 normal HCl to a pH of 2.9, using Töpfer's reagent (dimethyl-amino-azobenzene) as the indicator. Samples from 24 dogs were titrated with 0.01 normal NaOH to a pH of 8.4, using phenolphthalein as the indicator. The amount of HCl required to counteract the buffering effect of the lavage solution was obtained by subtracting from the total used the amount of HCl which would be required to carry a NaOH solution through the same pH change. The amount of NaOH required to counteract the buffer capacity of the lavage solution was obtained by subtracting from the total used the amount which would be required to carry a HCl solution through the same pH change.

RESULTS

The determinations of the buffering capacity and the pH within each segment are illustrated in Figs. 1 through 3. The figure plotted is the average obtained from the series of animals used.

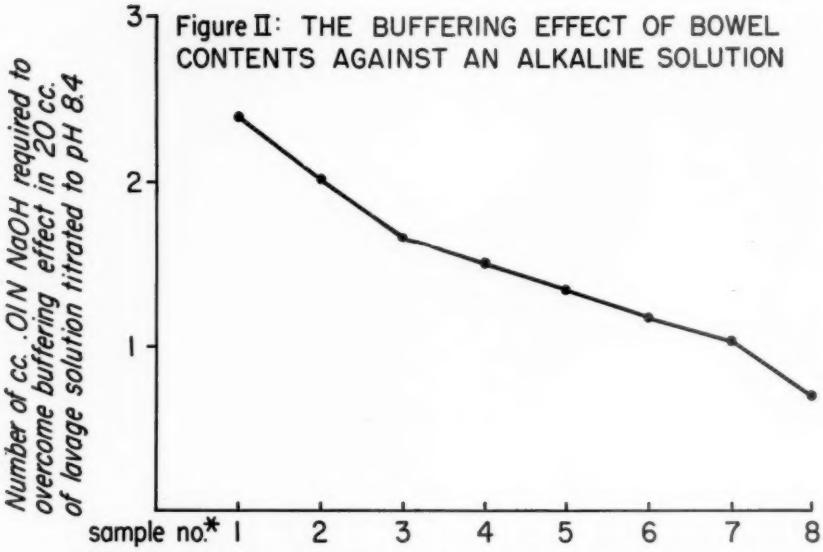
Figure II: THE BUFFERING EFFECT OF BOWEL CONTENTS AGAINST AN ALKALINE SOLUTION
Number of cc. .01 N NaOH required to overcome buffering effect in 20 cc. of lavage solution titrated to pH 8.4
3
2
1
sample no.* 1 2 3 4 5 6 7 8

*Each sample represents a 10 cm. segment of intestine analyzed. Sample no. 1 represents the segment 3 to 13 cm. distal to the pylorus. Sample 8 represents 10 cm. segment at 73 to 83 cm.

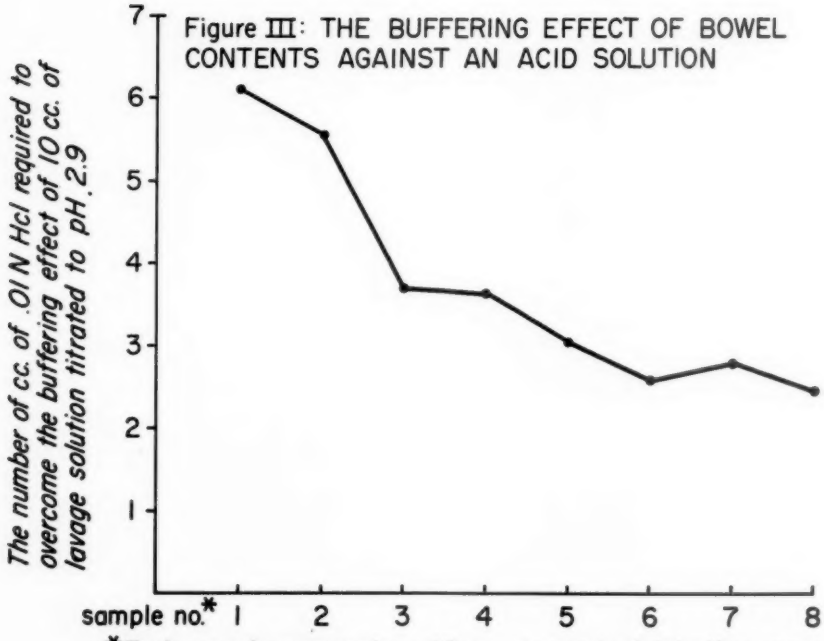
Figure III: THE BUFFERING EFFECT OF BOWEL CONTENTS AGAINST AN ACID SOLUTION
The number of cc. of .01 N HCl required to overcome the buffering effect of 10 cc. of lavage solution titrated to pH. 2.9
7
6
5
4
3
2
1
sample no.* 1 2 3 4 5 6 7 8

*Each sample represents a 10 cm. segment of intestine analyzed. Sample no. 1 represents the segment 3 to 13 cm. distal to the pylorus. Sample 8 represents 10 cm. segment at 73 to 83 cm.

The average pH of the lavage solutions obtained at 10 cm. intervals varied from 7.14 to 7.29 in the first 83 cm. of the bowel. There appeared to be a progressive decrease in the alkalinity of the contents as the distance from the pylorus was increased (Fig. 1). The first 10 cm. segment had the highest pH. This would appear reasonable, since the ampulla of Vater and the pancreatic ducts empty into this segment. In the dog, the major pancreatic duct empties singly into the duodenum, while the minor duct enters with the bile duct. Even though the animals were fasted eighteen hours prior to the test, and the hepatoduodenal ligament was clamped, it must be assumed that some pancreatic juice entered the bowel after the clamps had been applied. A sudden rise in the pH in the eighth sample, in the 10 cm. segment at 73 to 83 cm. distal to the pylorus, was noted. The reason for this occurrence is not known. The rise in the pH was not supported by similar changes in the buffering capacity (Figs. 2 and 3). However, the pH alone is not an indicator of buffering capacity of any solution.

The results shown in Figs. 2 and 3 indicate that the buffering capacity of the contents of the duodenum and jejunum decreased progressively as the distance from the pylorus increased. This decrease appears almost linear. The buffering capacity of the contents in the first duodenal segment was approximately two and one-half times that in the segment 73 to 83 cm. distally. This relationship was essentially the same against acid and alkaline solutions. In turn, the capacity against an acid solution, as plotted in this experiment, was approximately five times that against an alkaline solution. However, the titration of the lavage solutions with HCl was carried through a wider pH range. The exact relationship of the buffering capacity of the lavage solutions against acid and base was not determined.

DISCUSSION

Buffers, by definition, are substances which, when present in a solution, maintain the latter at a relatively constant pH when an acid or an alkali is added to it. In short, a buffer has the power to "soak up" or "tampon" acid or base. Because of the multiplicity of substances found in the juices in the region of the ampulla of Vater, the buffering system is undoubtedly very complex in nature. From this, it may be assumed that the complete "buffer system" has multiple isoelectric points, and therefore prevents any precipitous change in pH. In the normal animal, the buffer system is present in the first portion of the duodenum, and as the acid juices enter they are neutralized before any major change in the pH of the local environment can occur. Consequently, the pH remains at or near the neutral range.

The progressive loss of buffering capacity as the intestinal contents traverse the bowel lumen is probably dependent upon several factors. It is not unlikely that the nature of the contents is altered by a two-way exchange of ions, variable in type and amount between the blood and intestinal contents.[6] Furthermore, no attempt was made in these studies to determine the ionic content of the lavage solutions obtained at various levels. The addition of mucosal secretions such as

succus entericus into the lumen would influence both the pH and buffering capacity of the bowel contents.

Cantarow and Trumper[7] stated that, under normal conditions, approximately 90 per cent of the bile salts entering the intestine is reabsorbed into the portal circulation by the lymphatics. If it is assumed that the remainder of the constituents of the juices are capable of being absorbed in a similar fashion, then the results obtained from these experiments and those of Cross tend to indicate that the majority of the absorption occurs in the proximal portion of the small bowel. Cross stated that there is a sharp drop in buffering capacity of perfusion solutions from the intestinal loops longer than 20 cm. The work herein reported indicates an almost linear decrease in buffering capacity as the distance from the pylorus is increased.

This pattern of the loss in buffering capacity of the bowel contents is important when the Billroth II plan of gastric resection is contemplated. In this circumstance, care must be taken to insure as short an afferent loop as possible. The effective buffering capacity of the loop contents delivered at the gastroenterostomy is less and less as the length of the afferent loop is increased. This same mechanism would be existent when a gastroenterostomy is performed without gastrectomy. In view of other results from this laboratory, which cast real doubt upon the thesis of differential intestinal sensitivity to acid-pepsin mixtures, and in view of the results of others, which seem to minimize the secretin factor in this regard, it appears to us that the buffering capacity of the intestinal contents delivered at the gastroenteric stoma is the most important protective mechanism against the development of stomal ulcer when the Billroth II plan of gastrectomy is carried out.

The rationale of a short afferent loop in the Billroth II plan of gastrectomy appears to be closely related to the fact that the closer the gastroenteric stoma is to the pylorus, the greater is the buffering capacity of the luminal contents, and therefore in this situation there exists the greatest protection against the development of stomal ulcers.

SUMMARY AND CONCLUSIONS

1. A series of pH and buffering capacity determinations was made of bowel contents found at various levels of the small intestine up to 83 cm. from the pylorus.

2. There is a progressive decrease in the pH and in the buffering capacity of the bowel contents as the distance from the pylorus is increased.

3. By increasing the length of the afferent loop in the Billroth II plan of gastrectomy, less buffering capacity is available for the neutralization of acid secretion at the gastroenteric stoma.

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AN ELUCIDATION OF THE INTESTINAL SENSITIVITY FACTOR AND THE DISTANCE FACTORS IN THE INCIDENCE OF STOMAL ULCER IN THE BILLROTH II TYPE GASTRECTOMY*

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THE importance of a short afferent duodenojejunal loop in the Billroth II plan of gastric resection has been emphasized.[7-10] Several possible theories have been propounded for the increased incidence of stomal ulcers when a long afferent loop is utilized. The factors conceived to be important in the genesis of stomal ulcer are as follows: (1) the secretin factor, (2) the factor of altering the effective neutralizing capability of alkaline juices the further they progress down the intestine from their portal of entry into the lumen, and (3) the sensitivity factor, implying an increased susceptibility of the mucosa of successively lower segments of the small intestine to injury by the acid gastric secretions.

Matthews and Dragstedt[4] studied the factor of intestinal sensitivity by anastomosing an isolated gastric pouch obtained from the greater curvature to various levels of the intestinal tract. They concluded that the chemical action of pepsin hydrochloric acid can by itself produce typical chronic progressive ulcer in the stomach, duodenum, jejunum, ileum, or colon, and further that the resistance of these organs to the digestive action of pure gastric juice decreases progressively from the stomach to the colon. McMaster,[6] following a series of experiments in which the intact stomach was anastomosed to various segments of small and large intestine, concluded that "the intestinal mucosa was increasingly more sensitive to gastric content from the duodenum to the colon." He found no duodenal ulceration following gastroduodenostomy. Following gastrojejunostomy, jejunal ulceration occurred in 45 per cent of the animals. Iliac ulceration developed in 80 per cent of animals after gastroileostomy. Each of ten dogs developed a marked hemorrhagic colitis subsequent to a gastrocolostomy. The longest survival of the latter group was twenty days. Kolouch[3] concluded, from a series of complicated experiments wherein he employed a long afferent loop so arranged as to insure complete intragastric drainage of the afferent loop contents, that it was difficult to separate out with finality the role of the various factors contributing to the development of stomal ulcers, and that the secretin factor could not be divorced completely from the "distance" factor.

A previous report by one of us (K. A. M.)[7] indicated that following a 75 per cent gastrectomy of the Billroth II type, an afferent loop less than 27 cm.

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long was unattended by complications, while the utilization of an afferent loop 27 cm. or longer frequently resulted in stomal ulcers in dogs subjected to histamine stimulation. Furthermore, as the length of the afferent loop increased so did the incidence of stomal ulcer. This observation has been substantiated by others.[3, 5]

While the three factors alluded to initially undoubtedly play roles of varying importance in such an experimental preparation, it seems unlikely that the secretin factor is significant quantitatively. On the other hand, the buffering capacity of the material presented at the stoma (in part influenced by secretin) and the inherent sensitivity factor appear to be of greater importance.

The present project was proposed to utilize the experimental preparation of a 75 per cent gastrectomy and alteration of the length of the loop in various manners which would allow the interposition of various segments of the small intestine to be used for the gastroenterostomy stoma.

In this fashion, it is possible to compare and separate the factors of the length of the afferent loop and the intestinal sensitivity as each influences the incidence of stomal ulcer following the Billroth II type of gastrectomy.

MATERIALS AND METHODS

Forty-five adult mongrel dogs weighing an average of approximately thirty pounds were operated upon. Anesthesia was effected by the intravenous administration of 15 mg. of Nembutal per pound of body weight. All surgical procedures were carried out aseptically.

Each animal was subjected to a Billroth II type subtotal gastric resection, 75 per cent by weight. A Hofmeister closure was made on the lesser curvature side, and the duodenum was inverted. All intestinal anastomoses were performed by the closed method, utilizing a single row of interrupted No. 60 black cotton sutures. The gastroenterostomies were made by the open technique, using two rows of interrupted No. 60 black cotton sutures. The stoma measured 5 cm. in length in each case. The jejunal segments to be tested for sensitivity were selected at a distance of 27 cm. (the critical length) or more from the inverted duodenal stump.

The group of 45 dogs was divided into three series of 15 each. Each series was subdivided into five groups of 3 dogs each. The constant factor in all animals was a 75 per cent subtotal gastrectomy following the Billroth II plan. The three major series to be listed differ in that the length of the afferent loop and the source of intestinal mucosa utilized in the gastroenterostomy are varied.

Series I (Fifteen dogs, Fig. 1, *A*).—The duodenum was transected 15 cm. distal to the inverted duodenal stump. A 10 cm. segment of jejunum, in each series of 3 animals, then was isolated from progressively lower segments of the intestine. The blood supply was preserved carefully to each segment. In the first group of 3 animals, the 10 cm. segment represented the area 27 to 37 cm. from the inverted duodenal stump. In each succeeding group of 3 animals, the jejunal segments were obtained at progressively lower levels by 10 cm. increments. In the fifth group of 3 animals, the jejunal segment represented the

area 67 to 77 cm. from the inverted duodenal stump. Each isolated jejunal segment was interposed between the ends of the transected duodenum, and anastomosed in an isoperistaltic fashion. The gastroenterostomy then was made into the proximal end of the transplanted jejunal segment. Thus, the afferent loop was kept constant at 15 cm., and consisted entirely of duodenum. The variable factor from group to group was the site of origin of the transplanted jejunal segment.

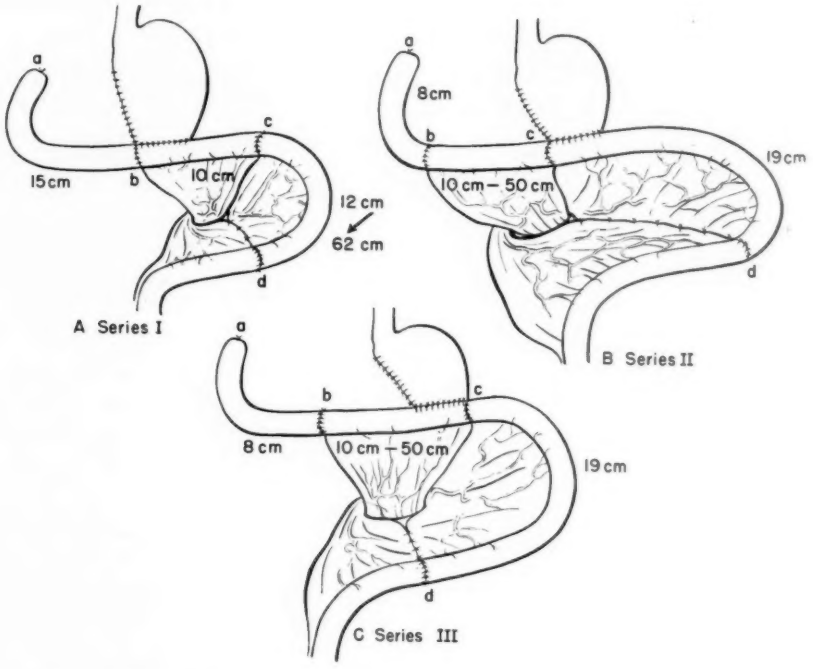

Fig. 1.—Schematic representation of the three plans of jejunal transplantation to test for differences in mucosal sensitivity to gastric juices. *a* to *b* is a segment of proximal duodenum. *b* to *c* is the transplanted jejunal segment anastomosed between the two ends of the transected duodenum. Segment *b* to *c* was obtained from site *d*. *c* to *d* is the distal portion of duodenum and/or the jejunum in normal continuity (see text).

Series II (Fifteen dogs, Fig. 1, *B*).—The duodenum was transected at a distance of 8 cm. from the duodenal inversion. In this series, the transplanted jejunal segment varied in length from 10 to 50 cm. In the first group of 3 animals, a 10 cm. segment of jejunum was isolated at 27 to 37 cm. distal to the duodenal inversion. In the second group, a 20 cm. segment was isolated at 27 to 47 cm. from the inversion. Progressively increasing lengths were isolated so that in the fifth group of animals, a 50 cm. length was isolated at 27 to 77 cm. from the inverted duodenal stump. Each jejunal segment was interposed between the two ends of the transected duodenum in an isoperistaltic fashion. The gastroenterostomy was made into the proximal end of the distal segment of the duodenum. Thus, the afferent loop varied in length from 18 to 58 cm. Each afferent loop contained 8 cm. of duodenum and a variable length of jejunum. In each case, the enteric portion of the gastroenterostomy consisted of duodenum

originally located at 8 to 13 cm. from the inverted duodenal stump; therefore, anatomically this represented a gastroduodenostomy.

Series III (Fifteen dogs, Fig. 1, *C*).—The plan in this series was the same as that used in Series II, except that the gastroenterostomy was made into the distal end of the transplanted jejunal segment. The afferent loop consisted of 8 cm. of duodenum and a variable length of jejunum. The loop varied from 13 to 53 cm. in length. Postoperatively, the animals were injected daily for four days with 150,000 units of procaine penicillin. Intravenous 5 per cent glucose was administered for two days, following which the animals were allowed milk, progressing to a routine kennel diet within seven days.

A postoperative recovery and rest period of at least forty-five days was allowed. The animals then were subjected to daily intramuscular injections of 30 mg. of histamine phosphate base in beeswax for a maximum period of forty-five days. The histamine-in-beeswax was prepared and injected in the usual fashion.[1] Injections were made at approximately the same time each evening. The animals were routinely fed between 2:00 P.M. and 3:00 P.M. each day. The food pans were allowed for approximately one hour after feeding time and then were removed. Water was allowed at all times.

All animals dying during, or being sacrificed at, the end of the forty-five day injection period were autopsied carefully. The ulcers were measured, and the residual stomachs were weighed. The weight of the remaining stomach pouch and the weight of the resected specimen were used to determine the percentage of gastric resection.

RESULTS

The results are briefly summarized in Tables I, II, and III.

Series I.—Each of the 15 animals received a total of forty-five injections of histamine phosphate in beeswax. There were no deaths. The animals were sacrificed twenty-four hours after the last injection. At autopsy, only minimal findings were noted. Superficial erosions of the esophageal mucosa were noted in 2 animals, and of the gastric mucosa in 1 animal. Petechial hemorrhages were found in the gastric mucosa of 1 animal. No stomal pathology was noted. These findings are considered important in that some of the gastroenterostomies were made with the jejunal segments obtained at a distance of 77 cm. from the pylorus.

Series II.—The results in this series varied. Histamine stimulation caused no effect in the animals with short afferent loops. However, as the length of the afferent loop increased, the mortality and severity of pathology increased. In the series of 15 dogs, there were seven stomal ulcers. This is of particular import when it is realized that the gastroenterostomy was anatomically a gastroduodenostomy of duodenum which in normal continuity was 8 to 13 cm. from the pylorus. It is of interest to note that 2 animals (C-20 and C-43) died due to esophageal complications. One of these animals had a large stomal ulcer; the other had no stomal ulceration. No stomal obstruction was noted in any case.

TABLE I. SERIES I. (FIG. 1, *A*.) SEVENTY-FIVE PER CENT GASTRIC RESECTION WITH THE GASTROENTEROSTOMY MADE TO THE TRANSPOSED JEJUNAL SEGMENT; EACH DOG WAS INJECTED DAILY WITH 30 MG. OF HISTAMINE-IN-BEESWAX

DOG NUMBER	WEIGHT (POUNDS)	SITE OF TRANSPOSED SEGMENT* (CM.)	LENGTH OF AFFERENT LOOP (CM.)	LENGTH OF SURVIVAL (DAYS†)	RESULTS
B-40	38	27-37	15	45	No findings
B-41	29	27-37	15	45	No findings
B-49	40	27-37	15	45	No findings
B-54	30	37-47	15	45	No findings
B-56	34	37-47	15	45	A few scattered petechial hemorrhages in the gastric mucosa
B-60	56	37-47	15	45	Several small superficial gastric erosions
B-61	38	47-57	15	45	Small superficial esophageal erosion
B-69	36	47-57	15	45	No findings
B-78	32	47-57	15	45	No findings
B-79	30	57-67	15	45	No findings
B-80	36	57-67	15	45	Two small esophageal superficial erosions
C-16	48	57-67	15	45	No findings
B-76	34	67-77	15	45	No findings
B-88	32	67-77	15	45	No findings
B-99	44	67-77	15	45	No findings

*Indicates the measured distance distal to the inverted duodenal stump. Each segment measured 10 cm. in length.

†Survival in days after beginning of daily histamine-in-beeswax administration.

TABLE II. SERIES II. (FIG. 1, *B*.) SEVENTY-FIVE PER CENT GASTRIC RESECTION WITH THE GASTROENTEROSTOMY MADE TO THE PROXIMAL END OF THE DISTAL DUODENAL SEGMENT; EACH DOG WAS INJECTED DAILY WITH 30 MG. OF HISTAMINE-IN-BEESWAX

DOG NUMBER	WEIGHT (POUNDS)	SITE OF TRANSPOSED SEGMENT* (CM.)	LENGTH OF AFFERENT LOOP (CM.)	LENGTH OF SURVIVAL (DAYS†)	RESULTS
B-100	42	27-37	18	45	No findings
B-98	42	27-37	18	45	No findings
C-17	37	27-37	18	45	No findings
C-4	30	27-47	28	45	No findings
C-14	30	27-47	28	45	0.5 cm. shallow stomal ulcer; no bleeding
C-39	32	27-47	28	45	Small superficial esophageal erosion
C-20	24	27-57	38	9	Perforated esophageal ulcer; deep indurated stomal ulcer
C-22	42	27-57	38	45	No findings
C-43	32	27-57	38	27	Large bleeding esophageal ulcer; no stomal ulcer
C-21	28	27-67	48	14	Perforated stomal ulcer
C-23	27	27-67	48	35	Large, bleeding and penetrating stomal ulcer
C-61	40	27-67	48	0‡	—
C-25	44	27-77	58	11	No pathology noted at autopsy
C-28	34	27-77	58	11	Perforated stomal ulcer
C-57	34	27-77	58	45	Large, chronic stomal ulcer

*Indicates the measured distance distal to the inverted duodenal stump. The segments varied from 10 to 50 cm. in length.

†Survival in days after beginning of daily histamine-in-beeswax administration.

‡Animal died on thirty-ninth postoperative day. Four large stomal ulcers (76 per cent gastric resection by weight).

TABLE III. SERIES III. (FIG. 1, *C*.) SEVENTY-FIVE PER CENT GASTRIC RESECTION WITH THE GASTROENTEROSTOMY MADE TO THE DISTAL END OF THE TRANSPOSED JEJUNAL SEGMENT; EACH DOG WAS INJECTED DAILY WITH 30 MG. OF HISTAMINE-IN-BEESWAX

DOG NUMBER	WEIGHT (POUNDS)	SITE OF TRANSPOSED SEGMENT* (CM.)	LENGTH OF AFFERENT LOOP (CM.)	LENGTH OF SURVIVAL (DAYS†)	RESULTS
C-100	44	27-37	13	45	No findings
K-14	34	27-37	13	45	No findings
K-16	28	27-37	13	45	No findings
K-12	32	27-47	23	7	Bleeding stomal ulcer; two small superficial esophageal erosions
K-3	38	27-47	23	45	No findings
K-19	40	27-47	23	45	Chronic stomal ulcer
K-8	32	27-47	33	27	Perforated stomal ulcer
K-9	32	27-47	33	45	No findings
K-11	30	27-47	33	10	Perforated stomal ulcer
K-5	44	27-67	43	45	Small stomal erosion
K-7	36	27-67	43	40	Chronic, bleeding stomal ulcer
K-15	50	27-67	43	45	Chronic stomal ulcer
K-2	32	27-77	53	9	Perforated stomal ulcer
K-3	34	27-77	53	30	Large chronic stomal ulcer
K-4	32	27-77	53	6	Bleeding stomal ulcer

*Indicates the measured distance distal to the inverted duodenal stump. The transposed segments varied from 10 to 50 cm. in length.

†Survival in days after beginning of daily histamine-in-beeswax administration.

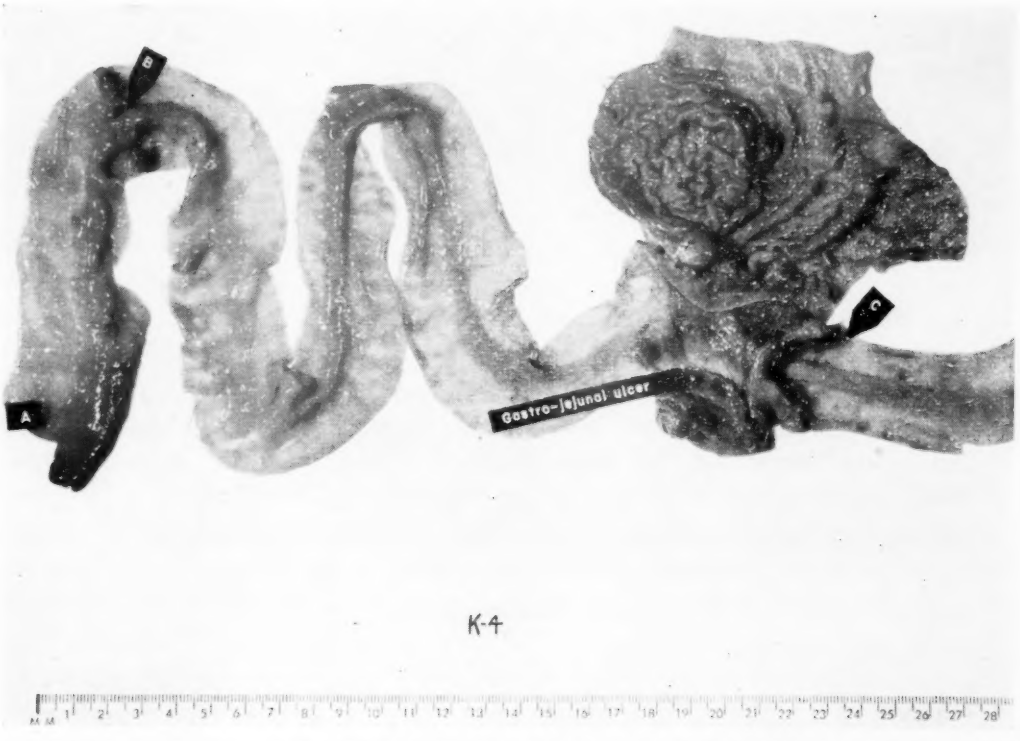

Fig. 2 (K-4, Series III).—Photograph showing a large stomal ulcer. *A*, Inverted duodenum; *A* to *B* represents 8 cm. of duodenum; *B* to *C* represents a 50 cm. segment of transplanted jejunum. Note that the ulceration does not extend to the anastomotic line. In no case did the ulcer involve the gastroenteric anastomosis. The reason for this is not known. It would appear, however, that avascularity was not a factor of ulcer formation since the enteric wall in juxtaposition to the anastomotic line has the poorest blood supply.

Series III.—This series of 15 animals underwent a similar procedure as Series II, except that the gastroenterostomy was made to a jejunal segment. The animals with short afferent loops tolerated the period of histamine stimulation well. The mortality and the incidence of stomal ulcers increased directly as the length of the afferent loop was increased. There were nine stomal ulcers in this group (Fig. 2).

DISCUSSION

The total lack of stomal pathology in Series I, wherein following a subtotal (75 per cent) gastrectomy the gastroenterostomy was fashioned with interposed jejunum obtained 27 to 77 cm. from the inverted duodenal stump, is of considerable importance. This experimental preparation parallels a previously reported series[8] wherein a gastrectomy of similar magnitude was performed with the gastrojejunostomy effected to identical jejunal segments, which however were in continuity, rather than interposed. The latter series resulted in a 100 per cent incidence of stomal ulcer, with a 43 per cent incidence of perforation with generalized peritonitis. The only difference between the series was the length of the afferent loop. In the present series it was constant at 15 cm. from the inverted duodenal stump, while in the early series the length of the afferent loop was dependent upon the site of the gastrojejunostomy. The striking contrast obtained by a comparison of these two series of experiments highlights the importance of a short afferent loop following the Billroth II plan of gastrectomy.

When the length of the afferent loop was increased as in Series II and III, the incidence of stomal ulcer increased pari passu in both series regardless of whether the gastroenterostomy was made to duodenum or jejunum as far as 77 cm. from the inverted duodenum. The incidence of stomal ulcer was practically the same in both groups of animals. It is of interest to note that in Series II, the gastroenterostomies were made to duodenum which originated only 8 to 13 cm. from the pylorus. The length of the proximal loop was the single variable factor.

One thing is certain, namely, that the secretions from the residual (25 per cent) gastric pouch delivered to the stoma have erosive potentialities. Furthermore, a protective mechanism or mechanisms are present which prevent stomal pathology when a short afferent loop is utilized.

These protective mechanisms have been alluded to previously. No definite conclusions may be drawn from these experiments regarding the secretin factor. However, if the entire duodenal mucosa is necessary for maximum secretin production, then the experimental preparations of McMaster, Dragstedt, and Matthews were ideal in this regard. In their preparations, the duodenum was intact. Consequently, the acid peptic juices, by implication, liberated an essentially optimal amount of secretin and therefore secondarily exerted a maximal protective action at the stoma. In view of the fact that stomal ulcers developed in their experiments with regularity, it must be assumed that the secretin factor is unimportant to this problem.

The results herein reported indicate that the factor of inherent intestinal mucosal sensitivity is likewise unimportant. While it cannot be assumed that segments of the small intestine lower than 77 cm. from the pylorus are relatively insensitive to gastric juice, certain facts should be presented which may not be apparent. The length of the dog's jejunum and ileum is approximately 290 cm. In man, the length of the small intestine from the ligament of Treitz to the ileocecal valve represents jejunum and ileum. Arbitrarily, the upper two-fifths is designated jejunum and the lower three-fifths is ileum. If these same relationships are applied to the dog, the jejunum extends 116 cm. from the ligament of Treitz. Therefore, the 10 cm. interposed loops obtained from 67 to 77 cm. levels represented small intestine exposed to acid juice from approximately the mid-jejunum. As evidenced by the results in all series, there is little, if any, evidence of increased mucosal sensitivity to acid peptic juice down to this level in the small intestine. Furthermore, recent experiments regarding the comparative sensitivity of the mucosa of the various segments of the gastrointestinal tract to acid peptic action in drip experiments indicate that there is actually little, if any, differential sensitivity in the entire small intestine.[2] Therefore, the factor of intestinal mucosal sensitivity seems to be of little or no importance with regard to the length of the afferent loop and the incidence of stomal ulcers.

By exclusion, then, one must concentrate primarily on the buffering capacity of the material delivered at the stoma as the major factor protecting against the development of stomal ulcers. In view of the increased incidence of stomal ulcer as the length of the afferent loop is increased, it must be assumed that the buffering capacity of bile, pancreatic, and bowel secretions is decreased the greater the length of bowel it must traverse.

Studies from this laboratory soon to be published[2] demonstrate that the buffering capacity of the bowel contents does actually decrease as the distance from the pylorus increases.

CONCLUSIONS

1. The importance of a short afferent loop in the prevention of stomal ulcers following the Billroth II plan of gastric resection has been reaffirmed.

2. Inherent mucosal sensitivity of the upper small intestine is relatively unimportant as a factor influencing the incidence of stomal ulcers under these conditions.

3. Contrary to previous opinion, the mucosa of the mid-jejunum does not appear to be more sensitive to gastric secretions than more proximal segments.

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THE COMPARATIVE SENSITIVITY OF THE MUCOSA OF THE VARIOUS SEGMENTS OF THE ALIMENTARY TRACT IN THE DOG TO ACID-PEPTIC ACTION*

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THE problem of gastrointestinal ulceration has been a subject of much discussion and investigation for many years. A matter of great concern to the surgeon is related to the recurrent or stomal ulcer attending operations specifically designed to cure the patient with ulcer diathesis. Such stomal ulcers occur in segments of the intestinal tract which rarely develop ulcerations "spontaneously." By subtotal gastrectomy in the Billroth II plan, a segment of intestine which in the normal situation is not subjected to the trauma of the acid-peptic mixture is placed in direct opposition to acid-producing mucosa. Furthermore, it has been shown that when the gastrectomy is made to progressively lower segments of the intestinal tract the incidence of stomal ulcer increases.[1, 2] This work suggests that there exists a differential susceptibility of the mucosa of the intestinal tract to injury, either chemical or physical. Consequently, segments of the gastrointestinal tract have been subjected to various physical and chemical agents in an effort to determine the degree of differential mucosal susceptibility or resistance to trauma at the various levels.[3-6] Kolouch[7] exposed the antral and duodenal mucosa, and made comparative studies on these two segments by exposing them to a drip of an acid-peptic mixture. He noted a marked difference in the reaction of the mucosa at these two sites. In this laboratory, attention has been drawn to the extreme degree of sensitivity of the esophageal mucosa to regurgitated gastric juices,[8] and to the lack of differential sensitivity of small intestine down to the mid-jejunum.[9]

Basically, the resistance to ulcer formation and the perpetuation of an ulcer once formed within a segment of the gastrointestinal tract will depend on the ability of the mucosa at that site to resist injury or, if injured, its ability to recover and heal. To our knowledge, no studies have been made evaluating the mucosal resistance of the esophagus, stomach, duodenum, jejunum, and ileum exposed to chemical trauma, and the ability of each of these segments to recover and heal. The problem to be resolved, then, is the differential susceptibility and the response to trauma of the mucosa at the various levels within the esophagus, stomach, and small intestine when exposed to an acid-peptic mixture.

MATERIAL AND METHODS

Twelve adult mongrel dogs were used. The animals were fasted for eighteen hours prior to surgery. They were anesthetized, using 15 mg. of Nembutal intra-

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venously per pound of body weight. Respiration was maintained by a mechanical respirator supplying oxygen.

A thoracoabdominal approach was used. The left thorax was entered through the tenth intercostal space, and the incision was extended distally across the costal cartilages and the abdominal wall. The left lung was retracted upward with wet laparotomy sponges. The diaphragm was divided from the hiatus in the direction of the thoracotomy incision. The lower esophagus was exposed at the cardiac juncture, and a 6 to 7 cm. longitudinal incision proximal to the esophagogastric sphincter was made on the left lateral aspect. The mucosa was exposed by elevation and the proper placement of a wet laparotomy sponge. A gastrotomy was performed to expose a segment of the gastric mucosa. A segment of the duodenum 10 cm. distal to the pylorus, the jejunum 10 cm. distal to the ligament of Treitz, and the ileum 10 cm. proximal to the ileocecal valve were exposed by making a longitudinal incision of similar length through the antimesenteric wall. This allowed the mucosa of the mesenteric wall of the bowel to be exposed.

In each case, a wet laparotomy sponge was placed so that the area exposed to drip was elevated and no "puddling" of acid-peptic mixture occurred at the exact site of the drip. The blood supply to each segment was carefully maintained. A black cotton suture was placed superficially in the serosa opposite the site of the drip. The suture served as a landmark to find the exact site of the drip at the time of autopsy.

An acid-peptic mixture of 0.1 normal HCl and 1 per cent pepsin was selected as the irritative "drip" solution since it has a pH of 1.2, approximately that of the gastric juice in the normal dog. One per cent pepsin was arbitrarily used. An increase in the percentage of pepsin up to 3 per cent does not appear to increase the irritative properties of the mixture. The acid-peptic mixture was dripped at the rate of 1 c.c. per minute to each of the five exposed segments. The mixture was dripped from burettes at a height of two inches. The excess of the drip mixture was absorbed by sponges, overflowed into the drapes, or aspirated from pools as it collected. The duration of the drip varied from fifteen minutes to fifteen hours.

An attempt was made to establish the optimal duration of drip. This would, of necessity, consist of a time interval which would produce mucosal damage of sufficient degree to evaluate both grossly and microscopically and yet not be so severe that a total lack of regeneration or healing would occur in the immediate postoperative period. Judging from the changes which occurred in the initial cases, it was felt that a drip period of sixty minutes would produce the desired specimens for study.

Three of the animals were sacrificed immediately following the experiment; the remaining animals were allowed to recover. The bowel incisions were repaired, and the peritoneal and pleural cavities were lavaged with warm saline solution. The chest and abdominal walls were closed in the usual manner. Procaine penicillin, 300,000 units, was given immediately postoperatively. Intravenous glucose solution was administered daily. The animal which was

allowed to survive for fifteen days postoperatively was eating a routine kennel diet by the fifth postoperative day. The animals were sacrificed at varied postoperative intervals.

Gross examination was made at the time of autopsy, and multiple sections were taken for microscopic study.

RESULTS

The results are briefly summarized in Table I. The application of the acid-peptic mixture by drip produced a similar tissue response at the corresponding levels within the alimentary tract in all animals.

Esophagus.—A thin layer of mucus covered the esophageal mucosa at the time of exposure. The layer persisted throughout the entire period of drip, even up to fifteen hours. Following the start of the drip, petechial hemorrhages appeared within the mucosa at approximately fifteen minutes. Blanching then occurred, followed by a translucent appearance of the superficial layers. The subepithelial vessels were observed grossly at approximately twenty minutes. The vessels darkened and appeared coagulated at approximately thirty minutes. Subsequently, the site of the drip darkened, but no new changes occurred during that period of exposure.

Animals were sacrificed at one, two, three, and fifteen days. All esophagi exhibited frank erosions or ulcers. In general, the site of injury appeared hyperemic, rough, and raw. Two animals (S-5 and S-10) had lesions covered by a plaque of necrotic tissue. A raw surface was found on dislocation of the plaque. Microscopic evidence of injury was noted in every instance. Definite changes were noted in the esophagi of the animals sacrificed immediately following the drip period. After fifteen minutes of drip, the stratified epithelium was absent over most of the drip site. Occasional islands remained. The lamina propria lost some cellular detail and became more homogeneous in appearance than is normal. The remainder of the esophageal structures appeared normal. After thirty minutes of drip, the epithelium was completely absent. The lamina propria was homogeneous in appearance and the blood vessels within it were distorted and coagulated. The lamina muscularis mucosae appeared normal, but the submucosa became distorted and areas of homogeneity with loss of cellular characteristics appeared. The most superficial portions of the esophageal glands lost cellular detail and regularity. Following fifteen hours of drip, evidence of severe injury was found. The entire esophageal wall was edematous, detailed cellular characteristics were absent, and all of the blood vessels were coagulated. The mucous glands appeared to be the most resistant to injury. Although the general contour of the glands was retained, the cellular detail was lost.

Evidence of esophageal injury persisted in the animals which were allowed to survive for variable periods postoperatively (Fig. 2). The edema and homogeneity noted immediately postdrip subsided, and the cellular detail became more apparent. Cellular infiltration was present twenty-four hours postoperatively and became more prominent at seventy-two hours. Small irregular areas of pale-staining squamous epithelium were noted at seventy-two hours. This was considered to be evidence of re-epithelization occurring from the margins.

TABLE I. A DIRECT COMPARISON OF THE SENSITIVITY OF THE MUCOSA OF THE ESOPHAGUS, DUODENUM, JEJUNUM, AND ILEUM TO ACID-PEPTIC ACTION

DOG NO.	DURATION OF DRIP IN MINUTES	POSTDRIP SURVIVAL IN HOURS (SACRIFICED)	POSITIVE FINDINGS OF INJURY AT AUTOPSY*					POSITIVE FINDINGS OF INJURY ON MICROSCOPY*				
			ESOPHAGUS	STOMACH	DUODENUM	JEJUNUM	ILEUM	ESOPHAGUS	STOMACH	DUODENUM	JEJUNUM	ILEUM
S-1	6,300 (15 hr.)	0	+	0	+	+	+	+	0	+	+	+
S-3	15	0	+	0	+	+	+	+	0	+	+	+
S-2	30	0	+	0	+	+	+	+	0	+	+	+
S-4	30	360 (15 days)	+	0	0	0	0	+	0	0	0	0
S-5	60	24	+	0	0	0	0	+	0	0	0	0
S-7	60	24	+	0	0	0	0	+	0	0	0	0
S-12	60	24	+	0	0	0	0	+	0	0	0	0
S-6	60	48	+	0	0	0	0	+	0	0	0	0
S-11	60	48	+	0	0	0	0	+	0	0	0	0
S-8	60	72	+	0	+	0	0	+	0	0	0	0
S-9	60	72	+	0	0	0	0	+	0	0	0	0
S-10	60	72	+	0	0	0	0	+	0	0	0	+

*Indicates gross and microscopic changes in structure as a result of injury. The changes are described in the text under Results.

The suture line was not bridged by epithelium at seventy-two hours. Microscopic study of the esophagus of the animal (S-4) sacrificed fifteen days after a thirty-minute drip revealed cellular infiltration through all layers. Infiltration was most marked in the submucosa. The epithelium showed regeneration, but had not covered the entire surface of the drip site. Complete epithelization had occurred across the suture line.

Stomach.—The area of stomach mucosa exposed to the drip mixture became covered by a persistent layer of mucus, and revealed no gross changes at the time of the exposure or at the time of autopsy. No changes were noted on microscopic study.

Intestine.—The mucosa blanched almost immediately following the start of the drip. No significant time difference was noted in the onset of blanching of the mucosa of the duodenum, jejunum, or ileum. Petechial hemorrhages appeared in the ileal mucosa in approximately two to three minutes, in the duodenal mucosa in approximately three to four minutes, and in the jejunal mucosa in approximately four to five minutes after the start of the drip mixture. The petechial hemorrhages remained for two to three minutes and then darkened as if blood coagulation had occurred. No further hemorrhaging appeared. The entire area of the drip became covered by mucus or mucinlike exudate shortly after the start of the drip. The area became progressively more necrotic in appearance. After approximately one hour, a small depression appeared at the site of the drip but never extended into the submucosal layers, even after fifteen hours. At the time of the autopsy of the animals which were allowed postoperative survival, only one lesion was noted on gross examination. A 4 mm. depressed, red area was noted in the duodenal mucosa of S-8. This lesion was not found in the sections taken for microscopic study.

Microscopic evidence of injury was noted in the small bowel segments in each animal sacrificed immediately following the experiment and in S-10, in which an ileal ulceration was found seventy-two hours postoperatively. In general, the findings of injury were very similar and indistinguishable in the duodenum, jejunum, and ileum.

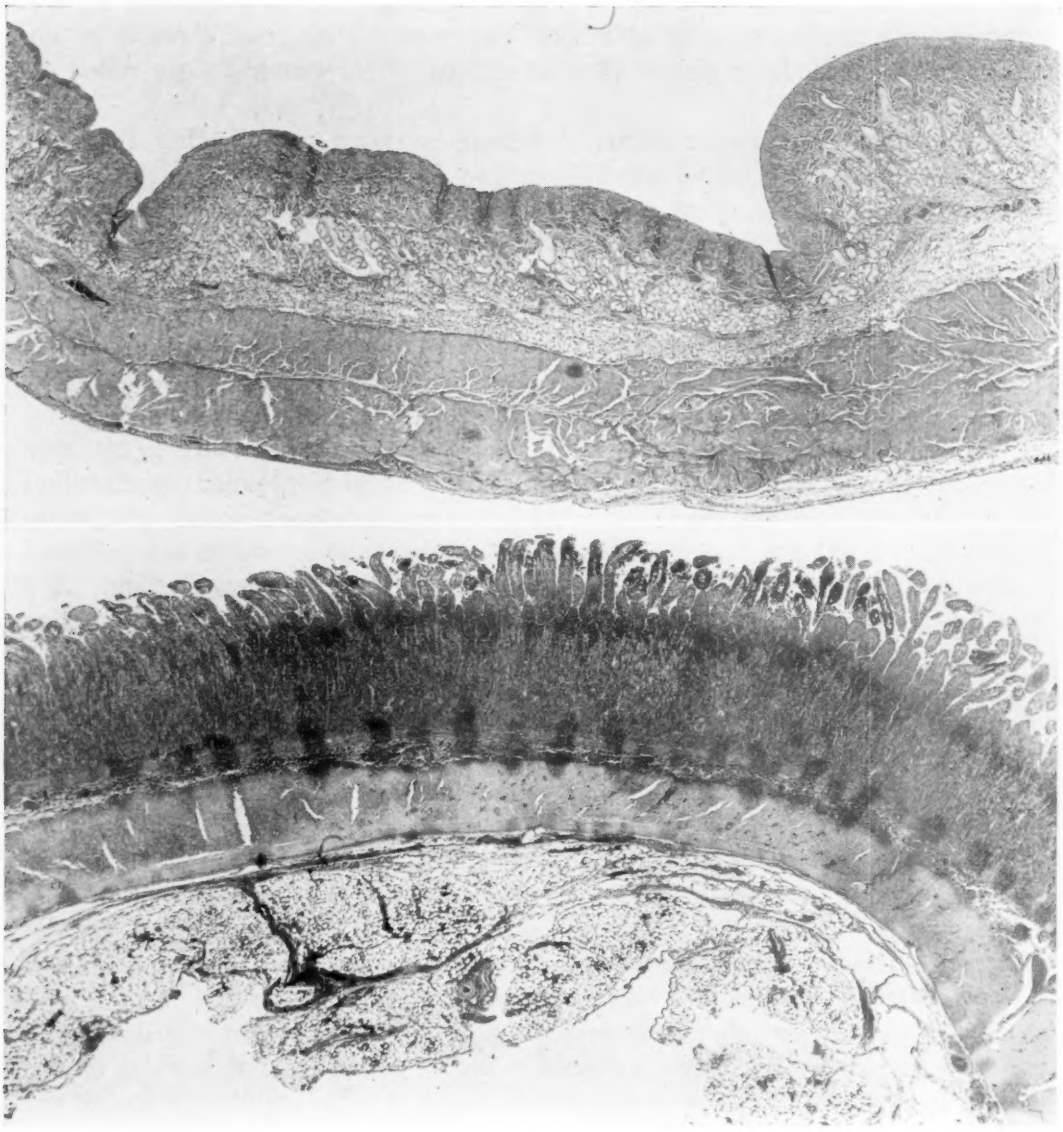
Following fifteen minutes of drip, the villi became distorted, and the most superficial parts were absent. Necrotic debris covered the surface. The remaining, superficial epithelial cells as well as the cells of the propria lost cellular characteristics and became more homogeneous. Evidence of extravasated blood was seen, but no coagulated vessels were noted.

Following thirty minutes of drip (Fig. 1, *A*, *B*, *C*, and *D*), the damage to the superficial mucosal layers increased. The erosion of the superficial epithelium and the lamina propria of the villi was marked. The capillary network and the central arteries and veins became damaged and appeared coagulated, taking a dark stain. The cellular detail was maintained in all remaining layers; however, the thickness of the bowel wall was increased, and in general a more homogeneous appearance was noted.

Following fifteen hours of drip, severe damage to all layers was evident. The villi were absent. The crypts of Lieberkühn became distorted and appeared empty and small as if dehydrated. The muscularis mucosae and the submucous

layers blended into one homogeneous distorted layer having no cellular detail. The muscular layers were distorted, homogeneous, and lacked cellular detail. The entire wall was thickened by edema. The blood vessels were identified, but the contents were homogeneous and represented destroyed and coagulated bloods.

A.



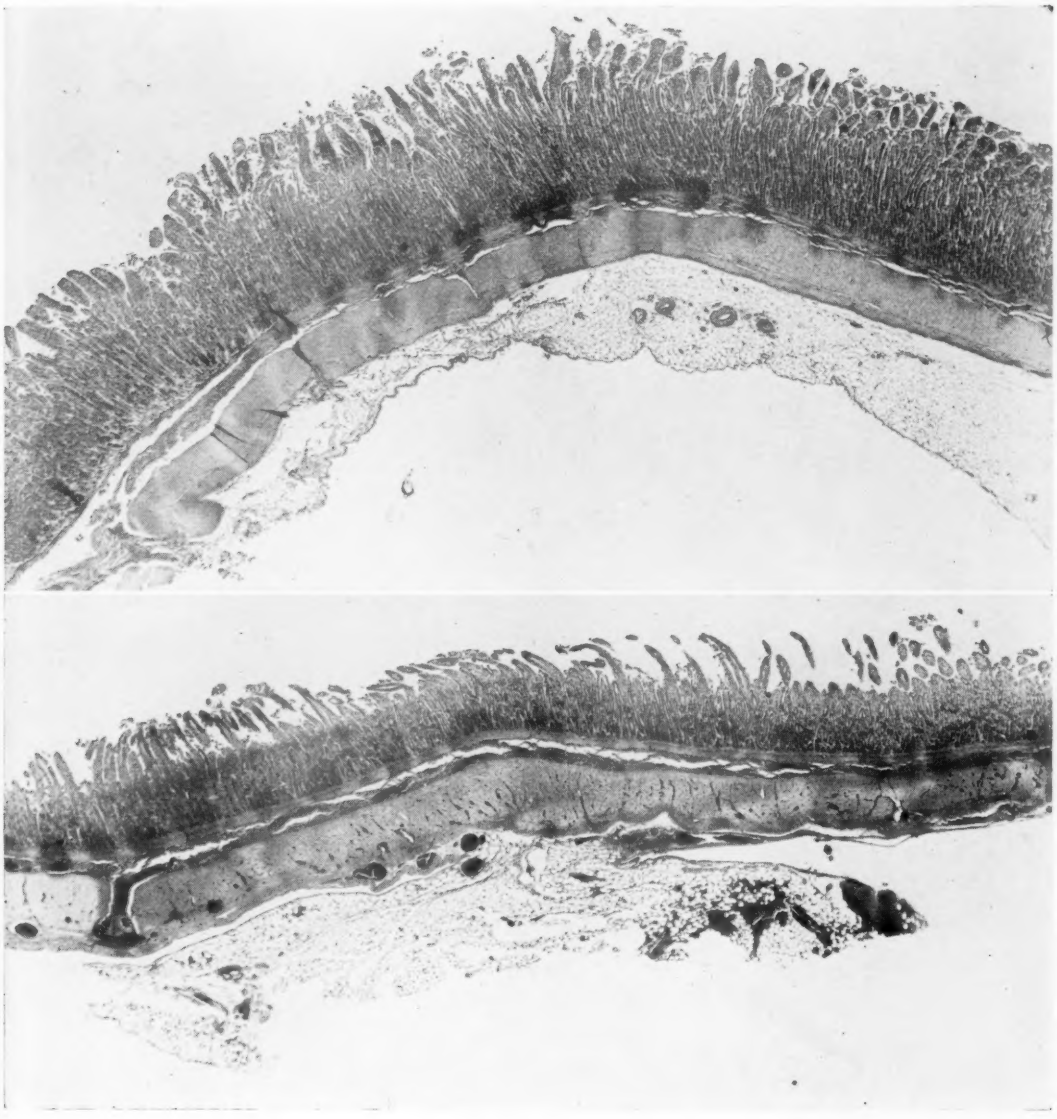
C.

Fig. 1.—Dog S-2. Photomicrographs of specimens exposed to thirty minutes of acid-peptic drip. *A*, Esophagus. Note the absence of the epithelium, the homogeneity of the lamina propria, and the coagulation of the surface vessels. *B*, *C*, and *D*, Duodenum, jejunum, and ileum. Note the distortion of the villi with loss of cellular characteristics of the superficial epithelium and lamina propria. Also, the superficial portion of the central blood vessels is damaged and takes a dark stain.

In the animals allowed to survive, microscopic evidence of mucosal injury was found in one instance only, S-10. This animal had been subjected to a

sixty-minute drip and was allowed seventy-two hours for recovery. At autopsy, an ulceration of the ileal mucosa was overlooked. Upon microscopy, however, complete denudation of the mucosa and an acute cellular infiltration of the mucosa were noted.

B.



D.

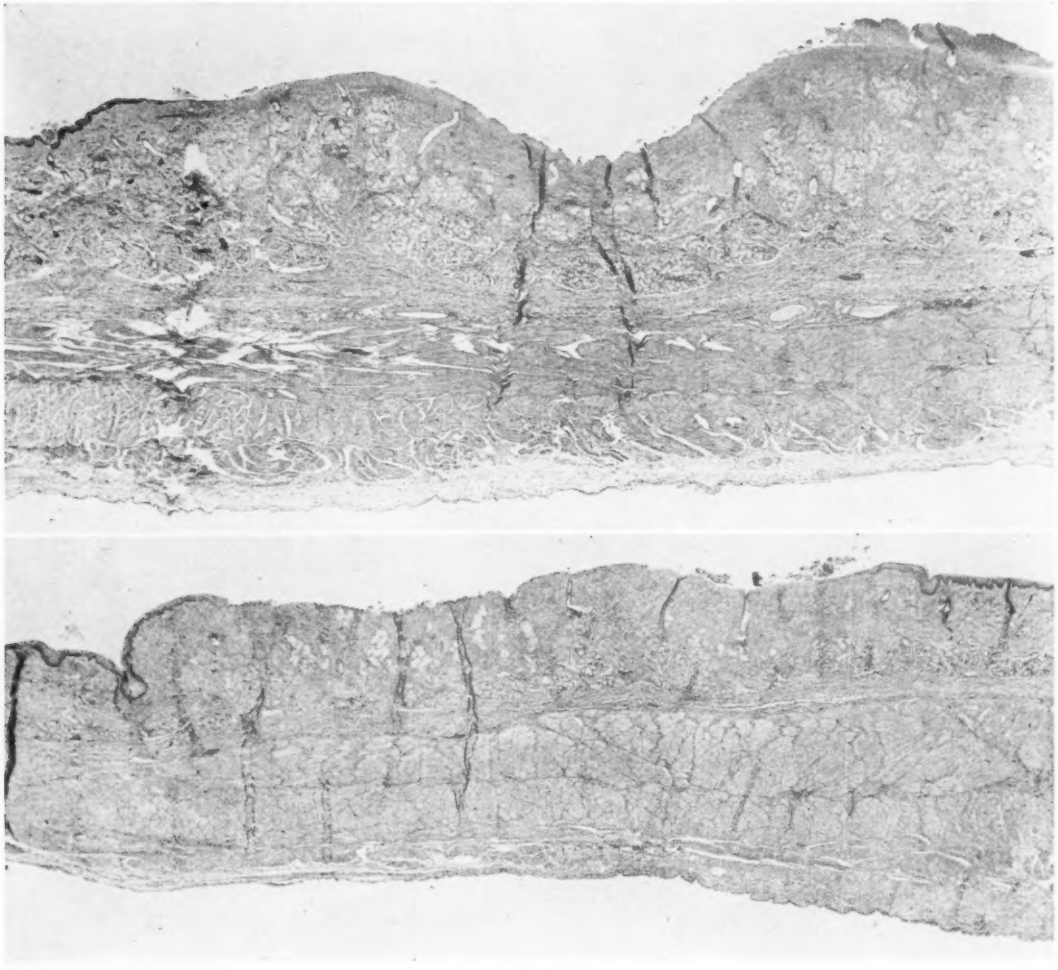
Fig. 1, *B* and *D*. (*For legend see opposite page.*)

DISCUSSION

The mucosal susceptibility to injury, either chemical or physical, at the various levels within the alimentary tract has been recognized. However, the extreme degree of sensitivity of the esophageal mucosa to acid-peptic injury has not been fully appreciated. The sensitivity of the esophageal mucosa to the

regurgitated gastric digestive mixture has been noted in this laboratory. Wangensteen,[10] an early proponent of the acid-peptic theory of the etiology of esophagitis, stated that the squamous epithelium of the esophagus is more vulnerable to injury by the acid-peptic digestive juice than is the glandular epithelium of the stomach. This statement may be expanded to include the small bowel.

A.



B.

Fig. 2.—*A*, Dog S-11, sacrificed forty-eight hours following a sixty-minute drip. Photomicrograph of the esophagus shows the epithelium to be absent. There is lack of loss of cellular detail in the lamina propria, lamina muscularis mucosae, and portions of the submucosa. Cellular infiltration is prominent, and a superficial necrotic plaque is noted. *B*, Dog S-10, sacrificed seventy-two hours following a sixty-minute drip. Photomicrograph of the esophagus shows similar changes as noted in *A*. Note the island of pale epithelium in the center. This is considered evidence of regeneration.

The ability of a mucosal surface to maintain "normality" depends on its ability to withstand insult or repeated irritative insults, and its ability to regenerate or heal. From the experimental work herein described, a comparative evaluation can be made of the mucosa of the esophagus, the stomach, and the

small bowel, as each reacts to the irritative properties of an acid-peptic mixture and as each responds in recovery. The mucosa of the stomach appeared very stable and showed no appreciable signs of injury either grossly or microscopically. Others have found the mucosa of the stomach to be very resistant to various forms of trauma. The mucosa of the small bowel was the first to show gross signs of injury. This appeared as "blanching," hemorrhage, and necrosis. However, the process was limited. The layer of mucus and cellular debris over the crypts may be the protective mechanism. The regenerative power of the small bowel epithelium is enormous.

The rapidity of regeneration of the mucosa of the small bowel is demonstrated in this experiment by the lack of gross or microscopic evidence of mucosal damage on examination twenty-four hours following a sixty-minute acid-peptic drip. The one exception was noted in Dog S-10.

It appears that the structural composition of the surface lining of the various sections of the alimentary tract is important. The glandular epithelium of the stomach was very resistant to injury. The mucosa of the small bowel consisting of villi and crypts was injured, but "healed" rapidly. No differential sensitivity of the duodenum, jejunum, and ileum to the acid-pepsin drip was observed either immediately or delayed. All responded in like fashion to the initial trauma and healed rapidly when the drip was discontinued. Apparently, the stratified squamous epithelium of the esophagus is very susceptible to injury by acid-peptic digestive mixture. Once injured, the regeneration is slow. This was demonstrated in this experiment by Dog S-4, in which mucosal regeneration was incomplete fifteen days following a thirty-minute drip.

SUMMARY

1. A method of studying the isolated effects of acid-peptic trauma to various segments of the alimentary tract has been presented.

2. This study revealed: (a) that the mucosa of the stomach is very resistant to trauma by an acid-peptic mixture; (b) that the mucosa of the duodenum, jejunum, and ileum is sensitive to acid-peptic injury, but that the injured area "heals" rapidly; and (c) that the esophageal mucosa is the most susceptible to injury and that the recovery rate is slow.

3. Under the conditions of this experiment, no significant differential sensitivity to the acid-peptic mixture was observed in the duodenum, jejunum, or ileum. All underwent similar changes in their initial response to the injury and in healing.

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THE EFFECT OF PARTIAL EXCLUSION OF BILE AND PANCREATIC JUICE ON THE ACIDITY OF THE GASTRIC CONTENTS IN THE POSTGASTRECTOMY PATIENT

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IN FOUR recent cases of duodenal ulcer patients subjected to partial gastrectomy plus vagotomy, we have utilized duodenostomy tubes as an added safeguard to hazardous duodenal stump closure. This preparation has afforded an unusual opportunity to study the neutralizing effect of regurgitant pancreatic, biliary, and duodenal secretions on the acidity of the gastric contents in the postgastrectomy patient. Opinions regarding the importance of enterogastric regurgitation in the modification of gastric acidity have varied widely. Most studies of this factor have been performed upon experimental animals, and in the majority, attention has been directed toward the development or prevention of jejunal ulcers in animals subjected to a variety of procedures which have aided or prevented regurgitation. Few such studies have been made in human beings, and only rarely have careful acidity studies been performed. We have been unable to find reference to another study similar to that reported here.

In 1923, the introduction of a method by which peptic ulcers could be produced in animals by the diversion of the duodenal contents to the lower small bowel[1] aroused considerable interest in the degree of protection against peptic ulcer afforded by the alkaline secretions contained in the duodenum. McCann[2] in 1929 reported the development of jejunal ulcers in 80 per cent of twenty-six dogs in which the method of anastomosis provided total regurgitation into the fundus of the stomach. He felt that jejunal ulcers could be as easily produced by introducing duodenal contents directly into the stomach as by draining them into the lower ileum. Methods reported by Graves[3] and Ivy,[4] however, in which duodenal contents were shunted into the antrum rather than the fundus failed to substantiate McCann's findings. Maier[5] modified McCann's procedure by anastomosing the proximal cut end of jejunum to the fundus of the stomach with a side-to-side anastomosis. In anastomosing the pyloric end of the stomach to the distal cut end of jejunum, both apposing ends were cut at an angle in order to obtain a large stoma and to interfere to some extent with the sphincteric action of the pyloric muscle. In McCann's preparation, the proximal cut end of jejunum was attached end to side to the gastric fundus, and the pyloric end of the stomach and the distal cut end of jejunum were joined with a simple end-to-end anastomosis. In Maier's hands, only one jejunal ulcer developed in several preparations, and he suggested

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that the discrepancy between his results and those of McCann might be explained by the fact that his maneuver provided for rapid emptying of the stomach due to the much larger gastrojejunostomy stoma, while in McCann's experiment the stoma was small, and delayed gastric emptying had been noted. Wilhelmj[6] further modified the duodenogastric drainage by creating a side-to-side anastomosis between the anterior gastric wall and almost all of the duodenum in such a way that the duodenum virtually formed a part of the anterior wall of the stomach. With this method, the development of jejunal ulcers was prevented. Owings and Smith[7] very logically carried the problem a step further, and having produced jejunal ulcers in animals using the Mann-Williamson preparation, they demonstrated that a certain percentage of these ulcers could be healed by shunting the duodenal contents back into the stomach. Lannin,[8] on the other hand, performed antral resection and established total regurgitation in four dogs, and found that jejunal ulcers developed in all.

Statements regarding the effect of enterogastric regurgitation on gastric acidity in the experimental animals are likewise contradictory. Neither McCann[2] nor Kesavalu and Mann[9] found significant change in the pre- and postoperative acidity curves after promoting intragastric duodenal drainage. Maier,[5] however, found considerable reduction in acidity in his animals after operation, while Wilhelmj,[10] who likewise found a reduction, concluded that the efficacy of duodenal secretions in lowering acidity is due more to dilution than to neutralization; "on the average 75 per cent of the reduction in acidity was due to dilution and 25 per cent to neutralization." Recently, Kanar and associates[11] have shown that in dogs prepared with Heidenhain pouches, gastroenterostomy resulted in a significant rise in volume and free-acid content of pouch secretion. Zubiran and co-workers[12] established Heidenhain pouches and then performed vagotomy. With this preparation, they demonstrated a rise in acid secretion by the pouch after gastroenterostomy in which the jejunum was anastomosed to the antrum. In animals in which they established a denervated Heidenhain pouch and, in addition, excised the antrum and anastomosed the duodenum to the distal end of the stomach, no change in acid secretion by the pouch occurred if the jejunum was then anastomosed to the body of the stomach.

Only a limited amount of evidence exists concerning the effect of duodenal secretions on the acidity of the gastric contents in man. Such evidence as is available is indirect in nature. Schmilinsky[13] is generally credited with the first attempt at total intragastric regurgitation in human beings. In a personal communication to Maier,[5] he described results in three patients with jejunal ulcer following posterior gastroenterostomy upon whom he reoperated and instituted total regurgitation. One died postoperatively, another died within one year of a new perforated jejunal ulcer, and the third developed a severe and distressing gastritis. An additional five patients with duodenal ulcer who were thus handled all developed severe postoperative gastrointestinal symptoms. Wangensteen[14] reported on three patients upon whom he performed antral excision with total intragastric regurgitation, with development of jejunal ulcers in two of the three. Cholecystgastrostomy has been

performed in an attempt to control gastric acidity by Babcock[15] and Braithwaite.[16] The latter described a recurrence of symptoms in 40 per cent of his cases within two years after operation.

Although total regurgitation has failed in human beings, this does not necessarily imply that the partial intragastric regurgitation which occurs after gastrojejunal anastomosis is an insignificant factor in the modification of gastric acidity. The possible importance of this factor is often minimized or overlooked in discussions of the effect of various maneuvers designed to reduce gastric acidity. Points more frequently stressed are complete antral excision, removal of a large segment of the acid-bearing portion of the stomach, removal of most of the lesser curvature, establishment of a short jejunal loop, and the possible beneficial effects of vagotomy. Although the bathing of the stoma by alkaline juices in high local concentration is recognized to have a protective neutralizing effect on acid gastric contents ejected through the stoma, the actual reduction of intragastric acidity by regurgitation may be of real importance in certain cases. We have recently[17, 18] pointed out our interest in the physiologic effect of various operative maneuvers on the acidity of the gastric contents, and have stated that if, as a result of operation, the pH can be maintained above 3.5 we believe the likelihood of recurrent ulceration is negligible. The evidence to be presented in this report suggests that in an occasional case the neutralizing effect of duodenal contents may be the deciding factor as to whether or not the operation performed fulfills our own criteria of acceptability.

METHOD OF STUDY

Our routine for the study of pre- and postoperative gastric acidity in ulcer patients has been previously presented.[17, 18] To recapitulate briefly, gastric contents are continuously aspirated and collected for one hour under "basal" or fasting conditions and for one hour after stimulation of the stomach by peptone beef broth. Sufficient intravenous insulin to effect a good clinical reaction is given, and four thirty-minute aliquots are collected over the course of the next two hours. With each aliquot, pH is detected using a Beckman pH meter, and free acid is determined by electrometric titration to a pH of 3.5. Above this pH level, no free acid is present. Volume is recorded and acidity is calculated in terms of total milliequivalent output per hour.

In two of the four patients referred to in this report, satisfactory preoperative studies were obtained, but in the others, massive hemorrhage necessitated emergency surgery and precluded routine evaluation. In each case, scarring, inflammation, and edema made dissection distal to the pylorus difficult, and resulted in an unsatisfactory duodenal stump closure. To protect against possible leakage, a Foley catheter was inserted into the duodenum through a stab wound distal to the suture line in such a way that the tip of the catheter lay near the ampulla of Vater. The Foley bag was inflated, and a purse-string suture applied to secure the catheter. In each case we removed an estimated one-half of the stomach and resected the vagus nerves below the diaphragm, a combination which in our hands has given more uniformly suc-

cessful results than any other procedure.[18] Convalescence was uneventful in each case. Postoperative studies were made both with the duodenostomy tube in place on suction and later, after its removal. Thus we obtained data concerning the acidity of the gastric contents during a period of at least partial exclusion of bile and pancreatic juice for comparison with values obtained when regurgitation, such as was afforded by the Hofmeister type of anastomosis, was taking place.

RESULTS AND DISCUSSION

Table I lists the pre- and postoperative acidity figures. Postoperative I values were obtained with the duodenostomy tube on suction and Postoperative II values, after its removal. Acidity is recorded in terms of pH and total milliequivalents of free acid per hour. The latter is calculated by the formula $\frac{\text{units of free acid} \times \text{volume}}{1{,}000}$. The volume of duodenal contents aspirated during the first postoperative studies is also tabulated.

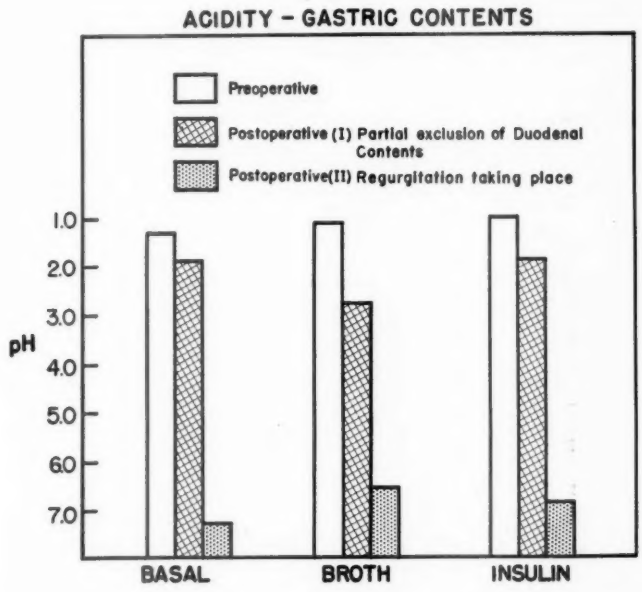
TABLE I. THE EFFECT OF PARTIAL EXCLUSION OF BILE AND PANCREATIC JUICE ON ACIDITY OF THE GASTRIC CONTENTS

		ACIDITY GASTRIC CONTENTS						
				POSTOPERATIVE I (WITH DUODENAL SUCTION)			POSTOPERATIVE II (WITHOUT DUODENAL SUCTION)	
		PREOPERATIVE						
CASE NUMBER	TEST	pH	MEQ. PER HOUR	pH	MEQ. PER HOUR	VOLUME OF DUODENAL CONTENTS ASPIRATED (C.C.)	pH	MEQ. PER HOUR
1 (E. R.)	Basal	1.3	5.3	1.9	0.24	21	7.3	0
	Broth	1.1	9.4	2.8	0.9	13	6.6	0
	Insulin	1.0	17.9	1.9	0.3	11	6.9	0
2 (M. L.)	Basal	1.4	4.4	4.0	0	12	6.5	0
	Broth	1.0	19.9	5.8	0	3	6.6	0
	Insulin	1.1	19.3	4.1	0	20	6.4	0
3 (C. S.)	Basal	–	–	3.7	0	2	5.2	0
	Broth	–	–	3.7	0	2	6.3	0
	Insulin	–	–	3.7	0	40	6.2	0
4 (H. C.)	Basal	–	–	6.0	0	7	5.2	0
	Broth	–	–	6.3	0	2	6.6	0
	Insulin	–	–	6.2	0	38	6.5	0

The values in Case 1 (E. R.) are most striking. With partial exclusion of the duodenal contents in the postoperative period it will be noted that the pH of the gastric contents is in a strongly acid range. Viewing these figures alone, one would say that the operation had failed to reduce gastric acidity to a point where recurrent ulceration could be considered highly improbable. The later studies, on the other hand, with regurgitation taking place reveal the gastric contents to be very nearly neutral. In this pH range, recurrent ulceration will almost certainly not occur. The reduction in acidity due to the presence of duodenal buffer substances is emphasized if hydrogen ion concentration is considered in terms of milligrams per cent. For example the

shift in postoperative pH under basal conditions from 1.9 to 7.3 represents a reduction in concentration from 1.3 to 0.000005 mg. per cent. We feel that it is unlikely that this marked difference in acidity, in otherwise identical studies performed five days apart in the postoperative period, is due to artefact. In our experience, the postoperative results check closely in the same patient tested at different times.

Fig. 1.



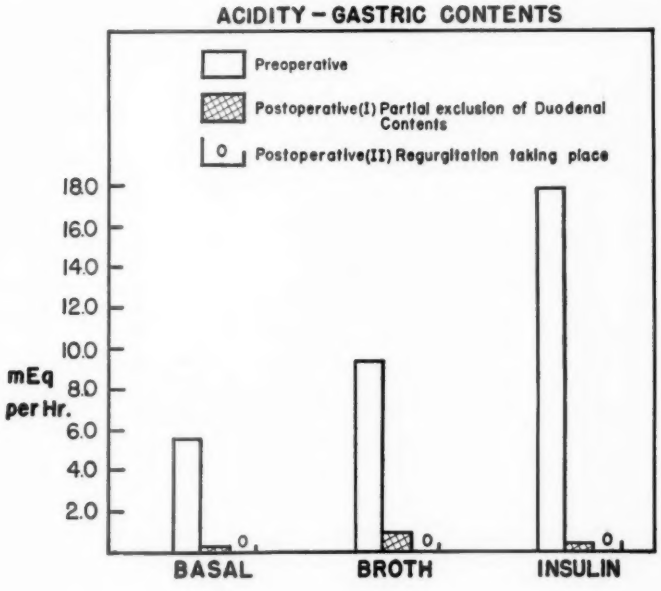


Fig. 2.

Fig. 1 (Case 1, E. R.).—The effect of bile and pancreatic juice on pH of the gastric contents following hemigastrectomy combined with vagotomy.

Fig. 2 (Case 1, E. R.).—The effect of bile and pancreatic juice on acidity of the gastric contents in terms of total milliequivalents of free acid per hour following hemigastrectomy combined with vagotomy.

The results in Case 1 are depicted graphically in Figs. 1 and 2. The marked quantitative reduction in acidity noted if the preoperative and Postoperative I values are considered in terms of total milliequivalents is due not only to some reduction in hydrogen ion concentration, but also to a marked reduction in volume of gastric contents. In Cases 2 and 3 (M. L. and C. S.), the results are less striking. The pH values in the first postoperative tests ranged between 3.7 and 5.8. In the second postoperative tests they were somewhat higher under all conditions of study. In Case 4 (H. C.), despite removal of a portion of the duodenal contents the postoperative pH levels were high.

The method of diversion of duodenal contents used in this study was such that a variable portion of the pancreatic and biliary secretions could proceed, unhindered, to the gastroenterostomy stoma. This probably accounts for the variation in the postoperative findings from case to case. Significant traces of bile were found in the gastric aspirations of Case 2, and to an even greater extent in Case 4. Failure of sufficient exclusion may well explain the high initial postoperative pH levels found in the latter case. In Cases 1 and 3, little evidence of bile was detected in the gastric contents. Although pancreatic juice unaccompanied by bile has been shown to reflux back through a normal intact pylorus,[19] it seems most unlikely that selective regurgitation would occur through a gastroenterostomy stoma, and therefore in Cases 1 and 3 diversion of the duodenal contents was apparently more effective.

We have previously indicated our satisfaction with the uniform reduction in gastric acidity effected by hemigastrectomy and vagotomy, a maneuver which, if properly performed, should largely eliminate both the chemical and neurogenic phases of gastric secretion. Among the patients discussed in this report, however, we would classify the physiologic results in Case 1 as poor and in Cases 2 and 3 as fair if we considered only the initial postoperative studies carried out with regurgitation prevented. On the other hand, all of the results based on the later postoperative studies with regurgitation permitted would be classified as entirely satisfactory. Small quantities of duodenal contents, seemingly insignificant in some instances, appear to have made a considerable difference. The volume which was diverted varied not only in different patients, but also from time to time in the same patient. The hourly volumes and the marked variation are not dissimilar to those recorded for biliary and pancreatic output under experimental conditions.[20] It appears that if the operative procedure performed greatly reduces the total amount of acid in the gastric contents by reducing both free acidiy and volume, as occurred in Case 1 (Fig. 2), but permits a small residue whose pH is low, this residue can be easily neutralized by a small quantity of bile and pancreatic juice. If, however, during the postoperative period there is a considerable volume of moderately acid gastric contents, then the small amount of buffer material regurgitated into the stomach might be completely overwhelmed with little or no change in gastric acidity. This would explain the results of Holman and Sandusky,[21] who found gastric acidity not appreciably altered in

92 per cent of seventy-five patients subjected to posterior gastroenterostomy, a procedure which provides regurgitation but either leaves unaltered or, according to some evidence, augments the mechanisms by which the stomach produces acid. It might further explain the failure of Schmilinsky's total enterogastric regurgitation and Wangensteen's enterogastric regurgitation plus antrectomy. It is to be borne in mind that duodenal ulcer patients, in general, produce large quantities of highly acid gastric contents both on fasting and under stimulation, but we have no evidence that in these same patients the production of bile or pancreatic juice is increased in a proportionate fashion. In a simple posterior gastroenterostomy, there is a single stoma between the stomach and jejunum which is the site of high local concentration of bile and pancreatic juice. In such a preparation, although gastric acidity may be insignificantly modified by regurgitation, sufficient neutralization takes place at the stoma to prevent gastrojejunal ulcers in the majority of instances. In total regurgitation procedures, the two stomas are separated from one another, and all of the duodenal contents are emptied into the stomach and diluted. As the quantity is probably insufficient to modify effectively the large volume of highly acid gastric contents characteristic of most ulcer patients, the full brunt of this acidity is then brought to bear upon the efferent stoma.

In Case 3, the initial postoperative pH values indicate achlorhydria but fall in a range in which peptic activity is not negligible. The relatively low hydrogen ion concentration is reduced to almost nothing when regurgitation is allowed. Peptic activity appears to become negligible when pH values are 4.5 or more.[22, 23] On the other hand, even though peptic activity may be significant in the range 3.5 to 4.5, we have yet to see a jejunal ulcer in a patient whose pH values were 3.5 or more under all of the conditions of study employed. To our knowledge, the old adage "no free acid, no peptic ulcer" is still valid.

SUMMARY

1. Suction applied to a duodenostomy tube inserted at the time of gastrectomy will remove at least a portion of the duodenal contents which normally bathe the stoma and regurgitate to a variable degree into the gastric lumen. We have studied postoperative gastric acidity in four such preparations with the duodenostomy tube on suction, and later after its removal.

2. In one case, diversion of bile and pancreatic juice appeared to have a profound effect on hydrogen ion concentration. In two others, the effect was slight but definite. In the fourth case, perhaps because of inadequate aspiration of duodenal contents, no appreciable change was noted.

3. Recurrent ulceration is highly unlikely if achlorhydria results from an operation performed for the relief of duodenal ulcer. The factor of regurgitation, frequently overlooked or minimized in discussions of the effect of various operative maneuvers on acidity of the gastric contents, may, in some instances, be decisive in the achievement of achlorhydria.

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THE RELATION OF BACTERIA IN THE BILE TO BILIARY DYNAMICS, CHOLANGITIS, AND POSTCHOLECYSTECTOMY SYNDROME

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IN PREVIOUS communications,[1, 2] one of us (J. M. McG.) has shown that many gall bladder patients demonstrate a sensitivity of the bile ducts to perfusion of normal saline solution under pressure. We have routinely measured perfusion pain pressure and resting intrabiliary pressure after gall bladder operations in patients with T tubes in the common bile ducts for over fifteen years. We have learned to expect a perfusion pain pressure of 550 mm. of water or more, and a resting pressure of 30 mm. of water or less. In most cases, the perfusion pain pressure is below the level of 550 mm. of water, and the resting pressure is above 30 mm. of water above the ensiform two weeks postoperatively. The biliary dynamics tend to reach normal levels after a period of T-tube drainage. The duration of drainage necessary to restore the "biliary dynamics" to normal is variable. We have come to learn that it is very essential that normal dynamics exist before the T tube is removed in order to avoid recurrence of biliary symptoms after operation.

With T-tube drainage, the biliary dynamics usually return to normal after variable periods, in some cases in six weeks, in others up to one year.

In two cases of cholangitis occurring postoperatively, we were impressed with the rapid return to normal of the biliary dynamics after injection of streptomycin through the T tube into the biliary tree.

These observations led us to believe that a low perfusion pain pressure indicated residual infection in the bile duct, that is, cholangitis. The pain produced by perfusion of the bile duct is of the same nature as pain which patients with biliary disease experience before surgery. For that reason we believe that a low perfusion pain pressure in the common bile duct indicates infection, that is, cholangitis.

Reasons for this belief are as follows: (1) pain on pressure is a cardinal sign of infection, and (2) invariably, tolerance to perfusion improves with common bile duct drainage, a fact in agreement with the surgical axiom that infection improves with drainage.

The purpose of this study, therefore, was to determine (1) the relationship between biliary dynamics and bacteria in bile, (2) the nature of bacteria in the common duct, and (3) the effect of antibiotic agents on (a) biliary dynamics and (b) bacteria in bile.

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Although there has been a great deal of research carried out on the bacteriology of gall bladder bile and to a lesser degree on duodenal drainage bile, there has been very little work of this nature reported on common duct bile.

REVIEW OF LITERATURE

Twiss[3] studied the bacteriology of the biliary tree. One hundred twenty patients with chronic biliary tract disease were studied. In each case a preoperative duodenal drainage was carried out with sterile precautions. A sterile duodenal tube covered with a gelatin capsule, so as to prevent contamination by organisms from the nasopharynx and laryngeal areas, was used. The basis of the study assumes that the normal fasting duodenum is sterile.

In 120 cases, Twiss found twenty-eight positive cultures from duodenal bile, and all of these were verified at operation. The organisms were found to be identical in the two types of cases. The types of bacteria found, in the order of frequency, were *Bacillus coli,* colon-Streptococcus group, *Bacillus typhosus,* nonhemolytic Streptococcus, Staphylococcus and Streptococcus, and an unidentified Enterococcus group.

Mirizzi[4] obtained bile for culture at operation by introducing an olive-tipped catheter through the stump of the cystic duct; in addition, he obtained bile from the gall bladder and duodenum, and cultured a piece of tissue from the gall bladder wall. He concluded that bile from the common duct is sterile in a large number of patients with disease of the extrahepatic biliary tract, and also that stone in the common bile duct is the most frequent cause of infection of the bile.

Zollinger and Cutler[5] emphasized the importance of *Bacillus coli* infection of the biliary tree. Of 146 patients operated upon for acute cholecystitis, four deaths were recorded, and the cause of death in three of these patients was infection. One had a definite septicemia due to *Bacillus coli,* and the other two had peritonitis due to the same organism.

METHOD OF STUDY

A series of cases of patients in whom T tubes had been placed in the common bile duct at the time of cholecystectomy was studied at the Boston City Hospital. The patients were seen at intervals of two to three days during the postoperative period, at which time the following studies were made: (1) cultures of the T-tube bile were taken, (2) intrabiliary pressure studies were recorded, and (3) the effect of antibiotics on the bacteria in bile was studied.

1. *Bacteriology.*—The bile was taken from the T tube by a sterile technique. The following method was found to be quite effective in excluding contamination after numerous bacterial checks: the exposed end of the T tube is washed with green soap, then alcohol (70 per cent), and finally painted with a 7 per cent tincture of iodine, with care being taken to paint the first 0.5 cm. of the inner portion of the T tube. After this has dried, another application of 7 per cent iodine is used. Then a 10 c.c. sterile syringe is attached to the prepared end of the T tube, and the bile allowed to enter the syringe at its own secreting pressure. About 3 to 5 c.c. of the bile is collected for culture.

2. *Biliary Dynamics.*—The biliary pressure studies were carried out by the method suggested previously by one of us (McGowan[6-8]). Briefly, the apparatus is assembled around an ordinary Y-shaped glass tube. The stem of the Y is attached by means of a rubber tube to a bottle of intravenous saline solution. To each limb of the Y tube is attached a rubber tube, one of which is to be connected to the T tube of the patient and the other to an upright manometer. The tubing is filled with normal saline solution from the reservoir bottle before it is connected to the patient, and all the air bubbles in the rubber tubing are removed. The zero level of the manometer is placed at the level with the xiphoid process of the sternum, with the patient lying flat on the back. Two separate pressure readings are made: (1) the resting intrabiliary pressure and (2) the perfusion pain pressure level.

The resting intrabiliary pressure is an index of the patency of the lower end of the bile duct. It is taken as follows: After the manometer is connected to the T tube as described, some saline solution is allowed to perfuse into the duct by allowing saline solution to flow from the reservoir bottle sufficient to raise the pressure to 100 to 200 mm. of water. The pressure is allowed to fall several times until an average level has been obtained. The resting intrabiliary pressure under normal conditions has been found to be less than 30 mm. of water above the xiphoid level. Elevated pressure may be due to various conditions, such as, inflammation of the head of the pancreas, spasm of the duodenal wall, a missed stone in the common duct, or edema of the duodenal mucosa at the ampulla of Vater.

If obstruction is due to spasm, it will be relieved by four deep inhalations of amyl nitrite. If this medication reduces the pressure to normal, the obstruction is due entirely to spasm. If it fails to do so, it is due to some other process. If there is a partial reduction of the resting intrabiliary pressure, then the obstruction is due partially to spasm and partially to a more permanent factor.

The perfusion pain pressure level is defined as the lowest hydrostatic pressure that the common duct can tolerate before the patient experiences discomfort. Some patients experience pain when the biliary tree is exposed to relatively low perfusion pressures at times not over 70 mm. of water, whereas in other cases pressures of 500 mm. and even 700 mm. can be tolerated without discomfort. This difference in pain pressure is explained as follows: If the bile ducts are dilated, high tension is developed by relatively low pressures; if the ducts are inflamed, the slightest intraductal pressure will produce pain. The bile passages should be able to withstand a pressure of 500 mm. without discomfort. If the T tube is removed while the perfusion pain level is below 300 mm. of water, subsequent distress can be expected. Previous experience has indicated that if the bile ducts are decompressed long enough by T-tube drainage, the tolerance to water pressure invariably improves up to 500 mm. of water or better. It is believed that the T tube can then be removed without the probability of postcholecystectomy syndrome. Experience with over 200 cases of T-tube drainage tends to bear this out.

Biliary pressure studies as described were carried out initially fourteen days after operation. We believe that studies should not be carried out before this time because of the danger of intra-abdominal leakage. The fistulous tract around the T tube at the end of fourteen days is well sealed off.

Biliary pressure studies were then carried out at least once and sometimes twice weekly depending on the individual patient. For the most part, patients were discharged from the hospital as soon as possible and then seen weekly at the Surgical Follow-Up Clinic.

Three criteria were used as an indication for T-tube removal: (1) *clinically,* the patient had no postoperative distress after the T tube had been clamped consistently for three weeks; (2) *bacteriologically,* bile cultures for pathogenic organisms were negative; (3) *physiologically,* the resting intrabiliary pressure was below 30 mm. of water and the pain perfusion level above 500 mm. of water.

3. *Antibiotics.—*

The administration of antibiotics intraductally was carried out in those patients who had a continual positive bile culture and a disturbance of biliary dynamics after fourteen days. Penicillin was instilled as 100,000 U. of aqueous type in 15 c.c. of sterile saline solution at least three times daily for two days, and then cultures were taken after twenty-four hours. The T tube was clamped off for two hours following each instillation. Streptomycin was also used in a few cases in doses of 1 Gm. four times a day, and instilled as described previously. Bacitracin was used also, but only as a preliminary study. Our aim in this paper is not to evaluate the relative merits of various antibiotics but instead to correlate the bacteriology with the biliary dynamics.

RESULTS

Twenty-seven cases of patients with T-tube drainage in all were used for this study. Twenty-one of these cases were studied in detail as far as the bacteriology of bile was concerned. Table I shows the quantity and types of bacteria found.

TABLE I. AN ANALYSIS OF THE BACTERIOLOGY OF BILE OBTAINED BY T-TUBE DRAINAGE

	NUMBER OF CASES	PER CENT OF TOTAL CASES
Cases with bacteria	18	85
Cases showing no growth	3	15
Total cases studied	21	
Cases with pure culture	2	10
Cases with mixed cultures	16	90
Total cases	18	
Types of organisms (in order of frequency)		
Escherichia coli	13	
Bacillus proteus	8	
Aerobacter aerogenes	6	
Bacillus pyocyaneus	5	
Bacillus welchii	3	

It is interesting to note that we had no growth of streptococci or staphylococci, which may be explained by the inhibitory effect of bile on these organisms.

Bile cultures were taken at various intervals ranging from the first day postoperative to as long as the sixtieth day. The cultures became negative at various time intervals. The average time was calculated to be thirty-five days after operation; this, of course, includes all cases regardless of whether the patient received any antibiotics or not. With the use of streptomycin in doses of 1 Gm. intraductally, four times a day for two days or eight doses, making a total of 8 Gm., the average time for negative bile cultures was about twenty-six days postoperative. Although this does not appear to be a great difference, each case must be considered individually because of the number of variable factors, such as, the age, duration, and severity of the disease, postoperative complications, whether or not there were stones, and finally the type and potency of the bacteria cultured from the bile.

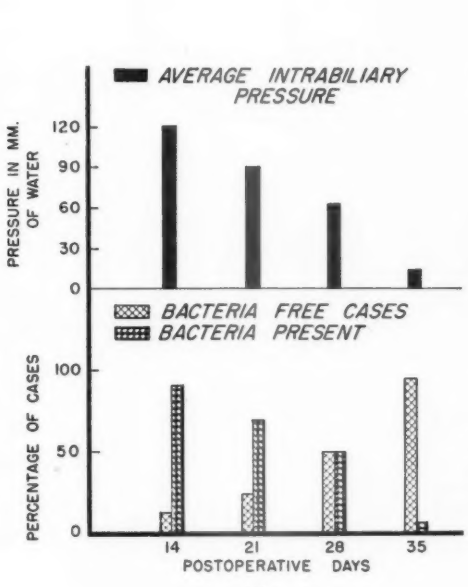

Fig. 1.

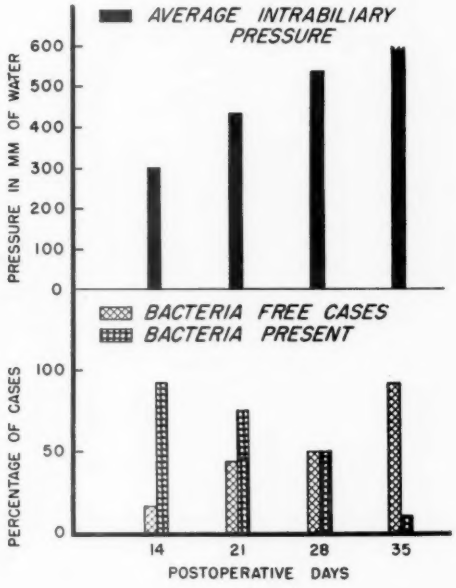

Fig. 2.

Fig. 1.—Graph representing the correlation between the average resting intrabiliary pressures and the bacteria of the bile in T-tube patients not receiving antibiotics intraductally. The intrabiliary pressures are resting ones and are averaged on the fourteenth, twenty-first, twenty-eighth, and thirty-fifth postoperative days. Note that on the twenty-eighth day one-half the patients have bacteria in the bile, and the resting intrabiliary pressure is above normal (30 mm.).

Fig. 2.—Graph representing the average pain perfusion levels as compared with the bacteriology of the bile in patients not receiving antibiotics intraductally. The pain perfusion levels are again average readings on the fourteenth, twenty-first, twenty-eighth, and thirty-fifth postoperative days. Compare with Fig. 4.

In comparing the relationship between the bile cultures, the resting intrabiliary pressure, and the pain perfusion level, there was a consistent and definite finding that when the bile cultures became negative, irrespective of how soon or whether or not antibiotics were used, the resting intrabiliary pressures and pain perfusion pressure were always within normal limits. The exceptions to the findings occurred in three cases in which the underlying pathology was chronic pancreatitis and carcinoma of gall bladder, respectively. In these three cases, there was a definite permanent obstruction to the lower end of the common duct. In all of these cases, the bile cultures became negative

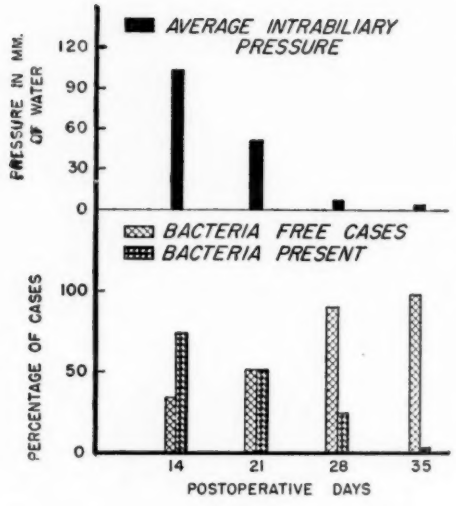

Fig. 3.

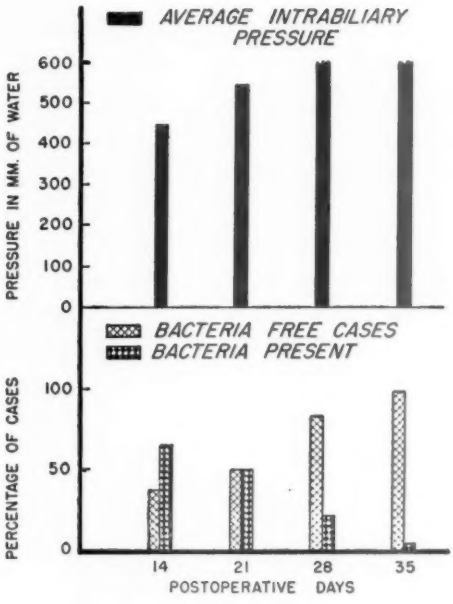

Fig. 4.

Fig. 3.—Graph representing the resting intrabiliary pressure correlated with the bacteria in bile in an average of patients who have received antibiotics intraductally. The averages are shown for the fourteenth, twenty-first, twenty-eighth, and thirty-fifth postoperative days. Compared with Fig. 1, the patients receiving streptomycin tended to be bacteria-free earlier, and the resting intrabiliary pressure tended to return to normal sooner.

Fig. 4.—Graph representing average pain perfusion levels correlated with the bacteria in bile in an average of patients who have received antibiotics intraductally. The averages are shown for the fourteenth, twenty-first, twenty-eighth, and thirty-fifth postoperative days. Compared with Fig. 2, one notes that there is increased tolerance to pressure in the duct by increased perfusion pain level and at the same time the patients tend to become bacteria-free sooner.

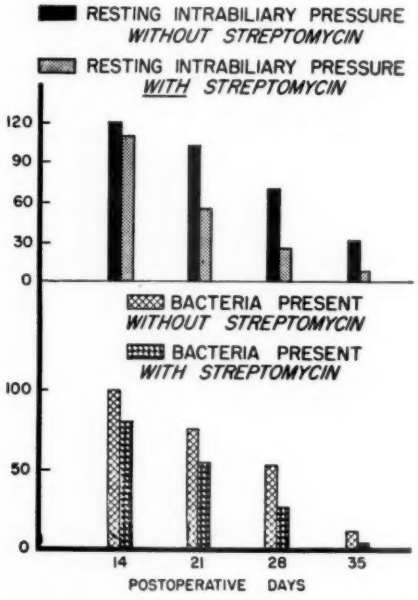

Fig. 5.—Graph representing a correlation of the resting intrabiliary pressures with and without streptomycin intraductally as compared with the bacteria in bile. The averages are from the fourteenth, twenty-first, twenty-eighth, and thirty-fifth postoperative days. The resting intrabiliary pressure tends to return to normal sooner in the patients receiving streptomycin through the T tube. Relaxation of spasm parallels disappearance of bacteria.

while the resting intrabiliary pressure remained elevated, while in sharp contrast the pain perfusion level was normal. In one of these cases, adenocarcinoma of the gall bladder had spread to the lymphatics about the common duct and caused an obstruction to the lower end of the duct.

Our findings are also represented by Figs. 1 through 4. We have attempted to show graphically the relationship between resting intrabiliary pressures, the pain perfusion levels, and the bacteria in bile on the fourteenth, twenty-first, twenty-eighth, and thirty-fifth postoperative days.

Figs. 1 and 2 represent the patients receiving no streptomycin and Figs. 3 and 4 represent those patients receiving streptomycin. It will be noted that as the bile cultures became negative in general, the resting intrabiliary pressure became normal, and likewise the pain perfusion level became normal. It will also be noted that in those cases in which patients received streptomycin intraductally the cultures tended to become negative earlier. A comparative study of both groups of cases is shown in Fig. 5.

Routine bile study forms were used for each case, which served as a very effective method of following the course of the patient postoperatively.

DISCUSSION

We have noted now for many years that patients with common duct drainage tend to improve, in so far as the biliary dynamics are concerned, on T-tube drainage alone. That is, the perfusion pain level, which may be low, as low as 70 mm. of water, postoperatively, will improve as drainage is continued, and on the other hand the ability of the patient to stand pressure within the bile duct improves. Concurrently with this, spasm of the lower end of the common bile duct tends to disappear.

The reasonable conclusions from these observations are: (1) Prolonged biliary drainage tends to permit cholangitis to improve, therefore increasing tolerance to intrabiliary pressure rises. (2) With improvement in cholangitis, a reflex spasm of the duodenal musculature tends to disappear.

The inferences which can be gathered from these observations are that the postcholecystectomy syndrome or biliary dyskinesia, so long known to be associated with spasm of the sphincter of Oddi, actually is secondary to infection in the upper radicles of the biliary tract, and the sphincter spasm is secondary as a result of reflex. If these conclusions are correct, then it would be expected that a shorter period of T-tube drainage would be necessary to restore biliary dynamics if antibiotics were used at the same time. In this paper, we are mainly concerned with correlating the bacteria in bile with biliary dynamics. The results have strengthened our opinion concerning the relationship of cholangitis to biliary dynamics. Also, the limited degree to which we have studied the effect of antibiotics administered parenterally and into the T tube tends to show that the duration of T-tube drainage is decreased with the use of antibiotics, that is, the patient's biliary dynamics return to normal sooner when they are used than when they are not.

The bacteriology of bile and its significance serve as a continual source of debate among workers in this field, as do the bacterial flora and its origin. For the most part, the organisms cultured are usually of enteric origin. This is easily explained when it is considered that any trauma or disturbance in the physiology of the common duct, cystic duct, and hepatic duct could encourage a retrograde spread of organism from the duodenum along the biliary tree.

The culture of *Clostridium welchii* from the bile has been obtained in many cases by other workers, as discussed previously. We have cultured this organism in a few cases, but only as a mixed culture and not as a pure culture. It is hard to evaluate the significance of *Clostridium welchii,* but clinically in those cases in which we obtained this organism, the patients were those presenting a history of symptoms extending over a long period of time, often associated with jaundice, chills, and fever in repeated attacks over a period of years.

There seemed to be a definite relationship between *Bacillus coli* and gallstones. In all of the cases of cholelithiasis, a positive culture of *Bacillus coli* was obtained from the bile. This observation is not a new one by any means; it has been previously noted that any obstructive element associated with the biliary tree, whether it be in the common duct or the cystic duct, seems to encourage the growth of *Bacillus coli.*

The intrabiliary pressure studies showed a definite correlation to the degree of infection in the biliary radicles. In those cases in which the bacteria in bile was abundant, the resting intrabiliary pressure was elevated above normal, and when the bacterial flora began to return to normal, the resting intrabiliary pressure returned to normal. Likewise, the pain perfusion level was also related directly to the degree of infection as manifested by the bacteria in bile. Patients who tolerated perfusion pressures up to 700 mm. of water without experiencing discomfort were found to have no bacteria in the bile.

A reduction in perfusion pain pressure below 550 mm. of water indicates the presence of infection in the bile ducts, that is, cholangitis. Supportive evidence includes these factors:

1. There is a correlation between low perfusion pain levels and bacteria; as bacteria disappears from the bile, the tolerance to pressure increases.

2. The perfusion pain pressure improves with T-tube drainage invariably. The measurement of perfusion pain pressure is the application of a basic principle in the study of the process of inflammation, no different from that employed by the clinician when he measures degree of inflammation in a felon by applying pressure with the examining finger.

The true role of antibiotics in our cases is hard to evaluate. Those patients receiving streptomycin intraductally had an earlier diminution of bacteria in bile than the controls. By the same token, the biliary dynamics were restored to normal much sooner. As to the relative value of different types of antibiotics, we are in no position to discuss this factor at this time. Study along this line is being continued by Dr. Walter Carrigan and one of us (J. M. McG.) at the Boston City Hospital.

As a practical clinical application concerning removal of the T tube, this work confirms what we have already shown, namely, that the T tube should be left in until (1) biliary dynamics have been restored to normal, that is, resting pressure is 30 mm. or less, and perfusion pain level is 550 mm. or more, and (2) cholangiograms show absence of stone or extrinsic pressure. Bile culture, while valuable in correlating data for research purposes, may not be necessary clinically, since results parallel biliary dynamics which are more easily measured.

SUMMARY

1. A review of the literature on the bacteriology of bile is presented.

2. A method of study of bacteriology of bile in T-tube patients is presented, with special emphasis on our method of collecting bile for cultures.

3. The biliary dynamics studies are described with recording of resting intrabiliary pressures and pain perfusion pressures in twenty-seven cases on T-tube drainage.

4. Twenty-one cases are reported in detail from the bacteriologic point of view. The most common bacteria found in bile were (in order of frequency) *Escherichia coli, Bacillus proteus, Aerobacter aerogenes, Bacillus pyocyaneus,* and *Bacillus welchii.*

5. Two of the common antibiotics, penicillin and streptomycin, were given intraductally to some of the patients. Their order of efficiency is as follows: streptomycin (most effective) and then penicillin. However, only a limited number of cases studied are here reported. Further studies are in progress, and at a later time more cases are to be reported.

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APPROACH TO MIDTHORACIC ESOPHAGEAL CARCINOMA FOR ITS RADICAL SURGICAL TREATMENT

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TO LOOK back on the history of esophageal surgery in Japan, the first reports on the radical removal of esophageal carcinoma were made in April, 1933, by our distinguished predecessor, the late Professor Seo, and by Professor Osawa at the Thirty-third Annual Assembly of the Japanese Surgical Association.

Since these reports were made, there had been no noticeable progress in this field of surgery in Japan until we succeeded in the radical removal of cancer of the lower thoracic esophagus by the abdominal approach in the use of so-called "*incomplete anastomosis*" with adaptation of esophageal tissue and gastric tissue by few sutures.

Since our first successful operation in February, 1946, the number of radical removals of thoracic esophageal cancers in the past seven years has amounted to 399 cases, including 101 cases of upper or midthoracic esophageal carcinoma (Table I). During these eight years, remarkable changes were made in the operative technique by the employment of positive pressure anesthesia and antibiotics which were introduced from the United States. Recently, we have succeeded in operating upon carcinoma of the thoracic esophagus almost as easily as performing gastrectomies in the past, in so far as the operative technique and operative mortality are concerned.

The operative methods applying to these carcinomas in our clinic differ according to the localities, and we have succeeded with each operative method, and we trust this report may prove worthy of consideration and reference.

Total or subtotal thoracic esophagectomy in the radical surgical treatment of upper and midthoracic esophageal cancer requires re-formation of the gastric tube as a secondary operative procedure in order to re-establish the continuity of the digestive tract.

Esophagogastric Anastomosis.—We have devoted especial attention in our cases of total or subtotal esophagectomy to the re-formed gastric tube in an attempt to clarify the question of where the gastric vessels should be ligated to avoid interference with or interruption of an adequate blood supply. We would like to report the results of this study.

Garlock and his associates have previously reported that necrosis of the stomach can be prevented if the right gastroepiploic artery alone is not ligated (Fig. 1). However, there was no report by these investigators describing details concerning any of the other gastric arteries in relation to the circulation of the stomach. We have noted that ligation of the right gastric artery excessively influences subsequent necrosis at the apex of the gastric wall (gastric cardia).

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Until recently, in our clinic, "antethoracic esophagogastric anastomosis" was employed as the routine operative procedure for re-establishing the gastrointestinal canal following total or subtotal esophagectomy. The subcutaneous gastric tube could thus be observed with comparative ease for the circulatory effects in question.

TABLE I. OPERATIVE CASES OF RADICAL ESOPHAGECTOMIES (FEBRUARY, 1946, TO JULY, 1953), NAKAYAMA SURGICAL CLINIC

OPERATIVE METHOD	TOTAL CASES	CANCER	ULCER	CORROSIVE STRICTURE	BENIGN STENOSIS
Cervical esophagectomy	13	13			
Total or subtotal esophagectomy	109	101	1	7	
Esophagocardiectomy intrathoracic esophagogastric or esophagojejunal anastomosis	80	73	2	1	4
Intra-abdominal esophagogastric anastomosis	48	41	4		3
Total gastrectomy with esophagectomy	140	130	10		
So-called incomplete anastomosis	48	41			7
Totals	438	399	17	8	14

Postoperatively, we have seen extensive necrosis of the gastric tube in three cases; this is illustrated in Fig. 2. One patient had a cicatricial healing of the gastric ulcer on the lesser curvature (Fig. 3) which had eroded through the blood vessels in this region. The other two cases were those of aged persons with a lesser curvature of short length but a long thorax. This necessitated individual ligation of the arteries along the lesser curvature to mobilize the stomach sufficiently to form a long gastric tube (Fig. 1). Such ligations were employed in other cases also. In most of them, a tiny necrosis or infection developed at the site of the anastomosis, which resulted in a small fistula extending to the skin. The patients who did not develop either the necrosis or infection subsequent to this type of ligation were relatively young people with better over-all circulation. On the other hand, where the method of individual ligation was not employed, none of the operative patients retained sufficient blood circulation of the mobilized gastric tube. This resulted in either necrosis or infection. Therefore, it is concluded that surgeons must apply the ligatures with great caution since improper ligation results in subsequent necrosis or infection of the mobilized gastric tube by virtue of inadequate gastric blood supply.

It is natural for surgeons to preserve as many gastric vessels as possible in order to prevent necrosis secondary to mobilization of the stomach. However, adequate mobilization for anastomosis of the gastric tube to the esophageal remnant requires extensive ligation of gastric vessels. With improper ligations, the hazard of unexpected operative death from necrosis or infection is great; this hazard may happen in the procedure which leaves only the right gastroepiploic artery unligated. The hazard is more marked when the length of the lesser curvature is short, thus requiring more extensive mobilization of this portion for the formation of the gastric tube, or when it is necessary to ligate the arteries along the lesser curvature in order to extirpate lymphatic metastasis in the celiac axis.

To determine more accurately the effects of various types of ligation procedures on the circulation of the gastric arteries, we have injected opaque

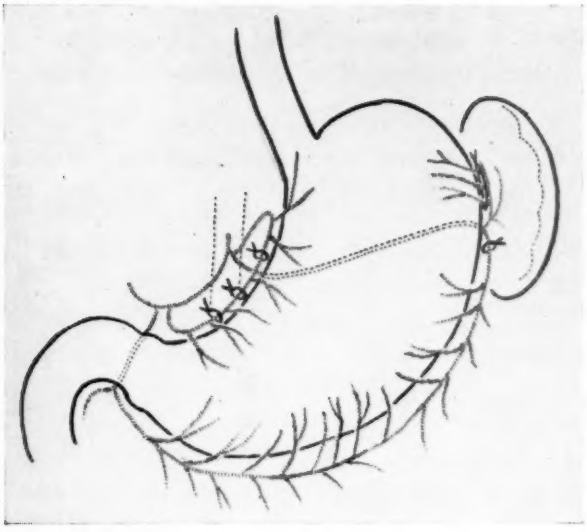

Fig. 1.—The right gastroepiploic artery is left, and the other gastric arteries are ligated. Each individual arterial arch along the lesser curvature is ligated.

Fig. 2.—Photograph showing the cicatricial healing of extensive necrosis of antethoracically mobilized stomach, and resultant fistula.

chemicals into one patent artery after the ligation of all other arteries in the stomachs of post-mortem specimens. This has been carried out in order to map the areas of stomach wall supplied by each of the various arteries involved.

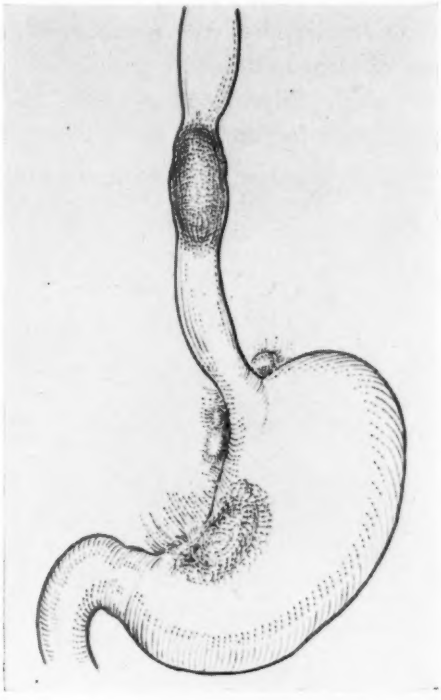

Fig. 3.—Midthoracic esophageal carcinoma with cicatricial healing of a gastric ulcer on the lesser curvature.

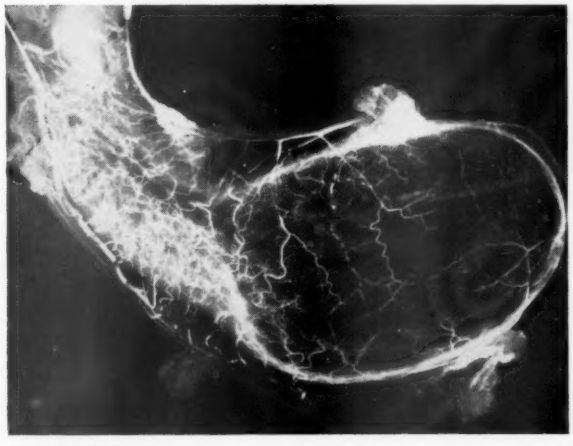

Fig. 4.—Roentgenogram of mobilized post-mortem gastric tube injected with contrast material into the right gastroepiploic artery following the ligation shown as in Fig. 5. Indicates that a sufficient amount of the material reaches the apical portion of the stomach.

As shown in Fig. 4, the mobilized gastric tube has a sufficient supply of the contrast material up to the apical zone following injection of the right gastroepiploic artery. In this instance, the arteries of the greater curvature and gastric cardia were all ligated, but the arteries of the lesser curvature were left

patent (Fig. 5). It is seen that it is not necessary to inject the right gastric artery in order to fill all the gastric arterial circulation, provided none of the branches of the right gastric artery are ligated.

In the second instance, we injected the right gastroepiploic artery with the opaque substance following ligations of the arteries along the lesser curvature (Fig. 6). Here again, we obtained sufficient supply of the substance up to the apical zone of the gastric wall. This demonstrates that the opaque substance injected into the right gastroepiploic artery flows into the apical portion of the mobilized gastric wall through the arteries along the lesser curvature (Fig. 7).

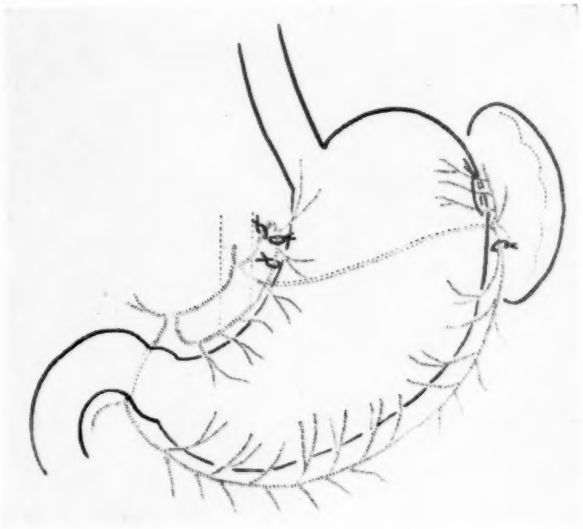

Fig. 5.—The right gastric and gastroepiploic artery are left.

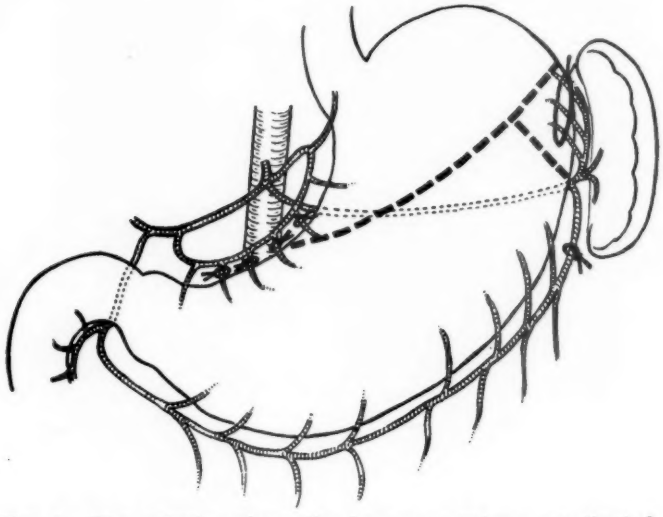

Fig. 6.—The arteries along the lesser curvature are ligated.

The third method of investigation was to ligate each individual arterial arch along the lesser curvature at the time of the mobilization of the stomach (as in Fig. 1). Injection of the contrast material into the right gastroepiploic

artery following such ligation shows only a very slight amount of the substance reaching the apical portion of the mobilized gastric wall (Fig. 8) as opposed to a sufficient supply as noted in the previous two instances. The results of this third investigative approach explain the high potential for extensive necrosis of the mobilized gastric wall when the procedure was carried out on aged persons with sclerotic arteries and poor circulation in general. Even necrosis may not occur; the circulation is so poor that the area can be easily infected, with resultant fistula formation.

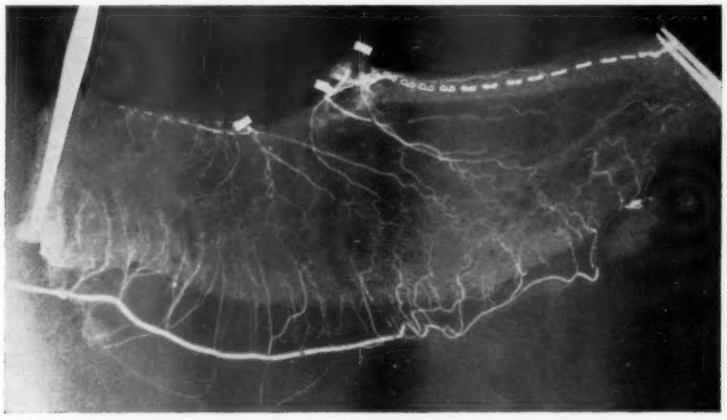

Fig. 7.—Roentgenogram of mobilized post-mortem gastric tube injected with contrast material into the right gastroepiploic artery following ligations of the arteries along the lesser curvature. The injected material flows into the apical portion through the arteries along the lesser curvature.

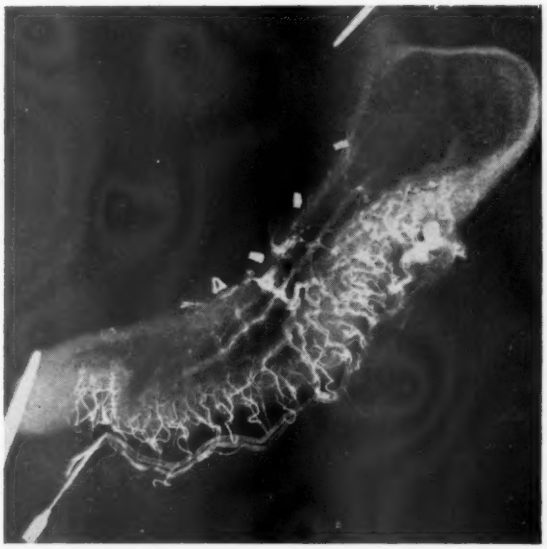

Fig. 8.—Roentgenogram of mobilized post-mortem gastric tube injected with contrast material into the right gastroepiploic artery following the ligation of the individual arches of the right gastric artery and other gastric arteries except the right gastroepiploic artery. Only a very slight amount of the material injected reached the apical portion of the stomach.

A considerable number of these fistulas was seen in previous cases. Therefore, we performed our total or subtotal esophagectomies using the antethoracic esophagogastric anastomosis or pulling the gastric tube up to the cervical

esophagus extrathoracically, thus making the anastomosis in the neck. This avoided intrathoracic anastomosis with the attendant danger of death from leakage through such fistulas into the thorax.

Another very interesting result was obtained in the investigation by injecting the opaque substance into the right gastric artery. The injection was performed after first ligating the right gastroepiploic artery at its axis, leaving the arterial arches along the lesser curvature untouched. The contrast material was seen to flow from the arteries along the lesser curvature to the arterial arches along the greater curvature, finally filling the vascular network in the apical zone of the mobilized gastric wall. Of course, the quantity of contrast material which flowed into the apical zone was visibly smaller than that in the former investigation.

Fig. 9.—Preoperative roentgenogram of midthoracic esophageal carcinoma.

The conclusion which became apparent from the results of these studies of the gastric circulation is as follows: In order to maintain sufficient blood circulation in the apical zone of the mobilized gastric tube in total or subtotal thoracic esophagectomy, it is essential for the surgeon to leave the arterial arches along the greater and lesser curvatures completely untouched, and to leave unligated either the right gastric artery along the lesser curvature or the right gastroepiploic arteries along the greater curvature.

The following case is presented in illustration.

CASE 1 (Figs. 9 through 12).—A subtotal esophagectomy with antethoracic placement of the stomach for esophageal carcinoma. In the operative procedure, the patient's right gastroepiploic artery was ligated at its axis, but arches of the arteries along the lesser and greater

curvatures were left untouched at the time of gastric mobilization. The patient recovered following the complete removal of the mid-esophageal carcinoma without the formation of any fistulas from the re-formed gastric tube.

The patient was a 41-year-old male physician who presented with a chief complaint of dysphagia. Clinical diagnosis was midthoracic esophageal cancer.

History of present disease: Three months prior to admission to the hospital, the patient noted retrosternal discomfort on swallowing. The condition progressed rapidly and caused the patient to visit the Medical College for examination on Jan. 12, 1951. By this time he could not swallow solid food. Fluoroscopic studies with accompanying radiographs showed signs of an esophageal cancer. He was sent to our clinic with this diagnosis and was admitted to the hospital on Jan. 25, 1951.

Fig. 10.—Removed specimen.

Examination on admission revealed a thin patient of medium height with hemoglobin, 85 per cent; red blood count, 4,200,000; white blood count, 6,700; urine, no specific findings; stool, positive for occult blood.

Surgery was performed on Feb. 1, 1951. The operative method was total thoracic esophagectomy with antethoracic esophagogastric anastomosis.

The patient was positioned face down for thoracotomy performed from the left thorax with resection of the fifth and sixth ribs. The carcinoma lay under the azygos vein, with infiltration toward the gastric cardia. An abdominal approach was therefore made by midline incision. Lymphatic metastases were found both at the axis of the celiac artery and at the

hiatus of the diaphragm. Another metastasis was found at the axis of the right gastroepiploic artery. In the process of extirpation of these lymph nodes, the gastroepiploic artery was ligated. Therefore, ligation of the right gastric artery was avoided. The anastomosis was made between the gastric tube and the esophageal remnant in the cervical region, with the tube raised antethoracically through a skin tunnel to the neck superficial to the sternum.

The postoperative course was uneventful and satisfactory. The patient was discharged from the hospital one month following admission without the formation of a fistula having taken place from the anastomosed part. The postoperative roentgenogram is shown in Fig. 11.

Fig. 11.—Postoperative roentgenogram which shows the re-establishment of alimentary tract with antethoracic esophagogastrostomy.

The operative handling of the gastric blood vessels was illustrated whenever total or subtotal esophagectomy required re-establishment of the continuity of the digestive tract by esophagogastric anastomosis which utilized the whole stomach for the gastric tube after complete mobilization. Recently, we have been applying the method of handling the gastric blood vessels suggested by the studies with the opaque material. This has been done so as to minimize the injury to the arterial arches along both the lesser and greater curvatures. Careful operative treatment of the gastric artery protects the anastomosis both from secondary infection and from fistula formation, thus helping to promote success in the primary cure accomplished by antethoracic esophagogastric anastomosis.

Let us now turn our attention to the problem of which operative approach is most advantageous for the complete removal of carcinoma in the mid- and upper-thoracic esophagus.

In the United States and Europe, MacManus, Kent, and Mathewson have been insisting upon the operative convenience of the right thoracic approach. However, this approach has a great disadvantage as compared to the left

Fig. 12.—Photograph of patient after operation.

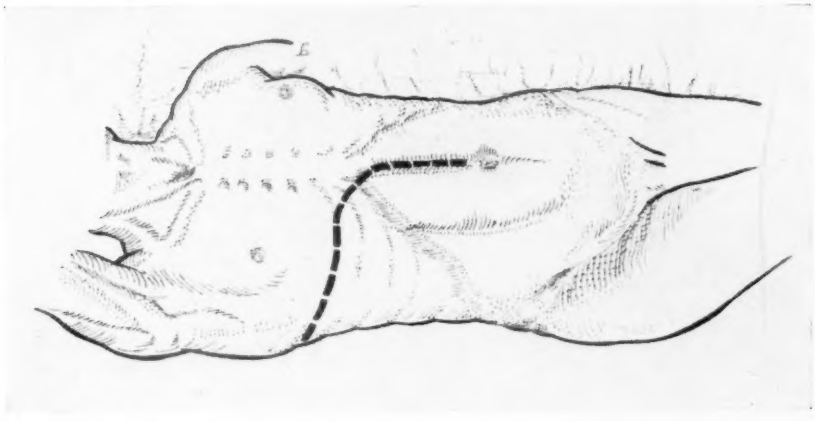

Fig. 13.—The dotted line shows continuous right thoracoabdominal incision.

thoracoabdominal approach, since the former requires two separate skin incisions, one from the abdomen and the other from the thorax. With this double incision, the difficulty is frequently encountered that, following the mobilization

of the stomach through the abdominal incision, the thoracic incision reveals an inoperable lesion lying in the thoracic cavity. The simultaneous approach from the right (thoracoabdominal approach) is similar to the procedure we have been using from the left to complete removal of carcinoma of the lower esophagus

Fig. 14.

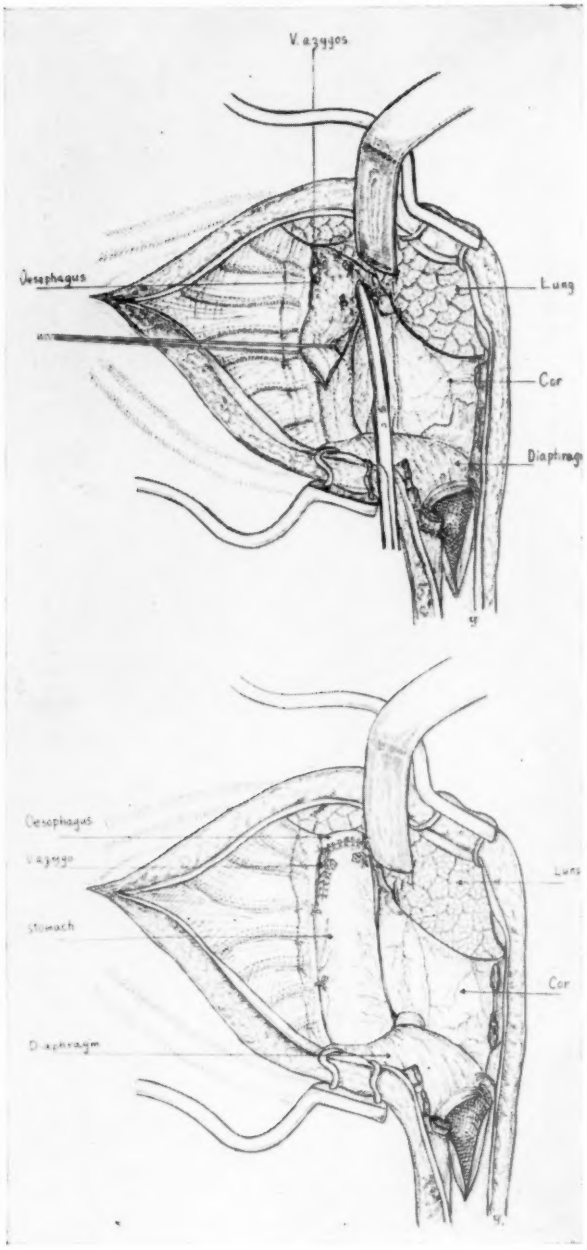

Fig. 15.

Fig. 14.—Diagram of completed anastomosis (right thoracoabdominal approach).
Fig. 15.—After ligation of the azygos vein, whole esophagus can be mobilized easily from the right thorax.

in a one-stage operation. This simultaneous approach from the right has been impossible and has resulted in objections by R. H. Sweet and others who prefer the left thoracoabdominal approach, even for the treatment of the upper and midthoracic esophageal lesions.

Since we have demonstrated, through our investigations just described, that the complete mobilization of the stomach can be carried out with ease and security, we have been struggling to establish a new approach from the right thorax for the radical surgical treatment of carcinoma of the upper- and midthoracic esophagus. We have finally succeeded in establishing a transdiaphragmatic approach from the right for the removal of carcinoma of the upper- and midthoracic esophagus. This approach eliminates both the costectomy and one unnecessary incision. It also simplifies the whole operative technique, while the approach from the left requires a blind operative technique for the removal of a lesion in this portion. The surgical procedures have been so simplified by this approach that the amount of bleeding during the operation has been reduced and the time for the entire operation has been amazingly shortened to approximately one hour.

Fig. 16.—Preoperative roentgenogram which shows midthoracic esophageal carcinoma.

Following is a brief explanation of the operative procedure: An incision is made from thorax to abdomen, as illustrated in Fig. 13, thus opening the thoracic and abdominal cavities through one continuous incision. Severance of the sixth and seventh or the seventh and eighth costal arches lays open the site of the lesion and allows us to identify the state of the malignant lesion in the thoracic cavity or the degree of the lymphatic metastasis at the axis of the

celiac artery in the abdominal cavity. This twofold evaluation can be performed at one and the same time. In addition, an evaluation of the gastric blood vessel arrangement may be made, and the mode of ligation can be decided upon. If it is seen that there is a likelihood that the operation may produce some interference with the blood circulation of the mobilized stomach, antethoracic esophagogastric anastomosis must be the procedure of choice to follow

Fig. 17.

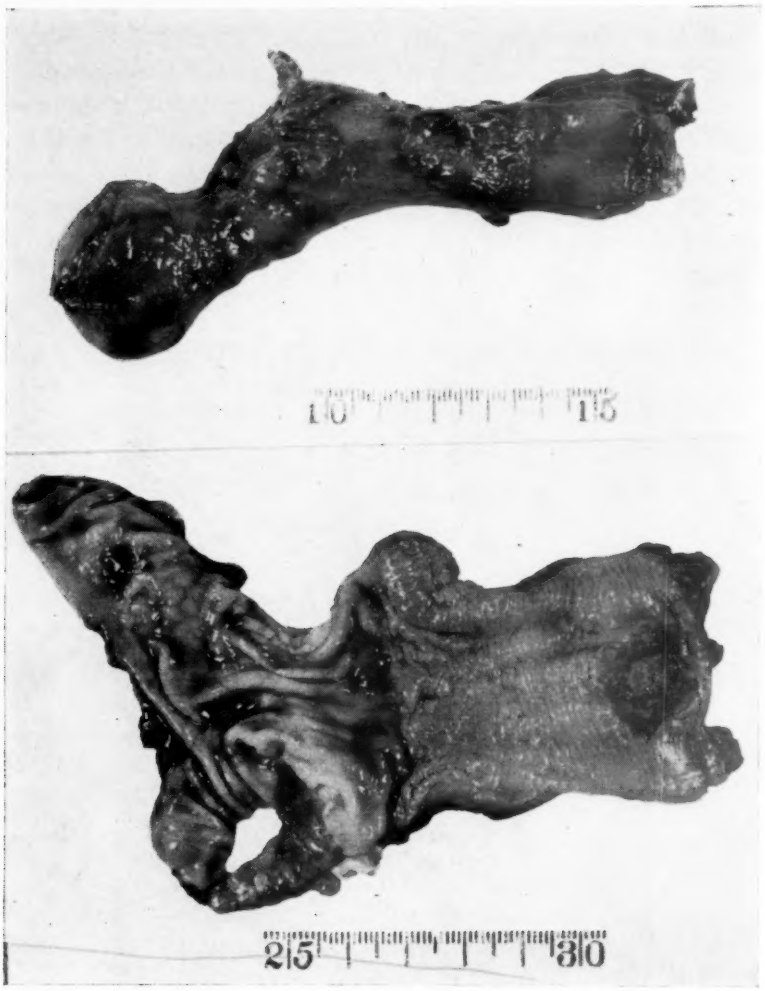

Fig. 18.

Fig. 17.—Outside of removed specimen.
Fig. 18.—Inside of removed specimen.

extirpation of the lesion. However, if the arrangement of the gastric vessels is such that it lends itself well to a ligation which leaves an adequate blood supply, then intrathoracic esophagogastric anastomosis is preferable.

The first step of the procedure within the abdominal cavity is the mobilization of the esophagus from its surrounding tissue, following the ligation and

division of the azygos vein (Fig. 14). The esophagus is then amputated above the level of infiltration, and the amputated esophagus is pulled to the abdominal cavity through the hiatus of the diaphragm. This is done without making an incision in the diaphragm.

Radical extirpation of the lesion after careful evaluation of the infiltrations is followed by mobilization of the stomach and fashioning of a gastric tube. The gastric tube is brought to the upper remnant of the esophagus through the hiatus of the diaphragm and positioned for anastomosis within the thoracic cavity (Fig. 15). Anastomosis of the posterior wall is carried out with one layer of suture (Albert). Three anchoring sutures are placed, which secure the posterior wall of the gastric tube to the mediastinal pleura or to the aortic adventitia. Interrupted silk is used. The anterior wall is usually anastomosed in two layers, Albert and Lembert suturing being used. The gastric serosa is united with the mediastinal serosa.

Fig. 19.—Postoperative roentgenogram demonstrating anastomosis being observed at the level of aortic arch.

(This technique for esophagogastric anastomosis is usually utilized in lower thoracic esophagectomy also.)

The thoracic and abdominal walls are closed by two layers of suture, following the insertion of a T tube into the thoracic cavity. A stomach tube is also inserted to be utilized both for suction of excess gas and fluids in the stomach and also for feeding purposes after the third postoperative day.

Recently, 22 cases (until July, 1953) of radical esophagectomies for middle and upper thoracic esophageal cancers have been performed, using this new approach. There has been no operative death in our clinic as yet.

CASE 2 (Figs. 16 through 20).—The patient was a 59-year-old man who presented himself with the chief complaint of dysphagia. Clinical diagnosis was midthoracic esophageal cancer.

Clinical history: The patient gave a history of dysphagia with onset three months prior to admission and with sudden increase in severity twenty days prior to admission. The patient experienced the feeling of stagnation of food and retrosternal burning. By the time of admission, the patient could not digest solid food.

On admission Aug. 30, 1952, examination revealed a man of medium height, but thin. Hemoglobin count was 75 per cent; red blood count, 4,000,000; white blood count, 7,800; stool examination, positive for occult blood. Operation was performed Sept. 5, 1952. The operative method was subtotal esophagectomy by the right transdiaphragmatic approach with intrathoracic esophagogastric anastomosis.

Fig. 20.—Photograph of patient after operation.

Operative findings: A malignant lesion of the esophagus was discovered at the level of the azygos vein. Infiltration of the lesion into both the anterior and the posterior wall of the esophagus was noted. Adherence of the lesion to the surrounding tissue was present, and lymphatic metastases were also found at the axis of the celiac artery. Following the extirpation of these lymph nodes, the esophagus was removed, together with a portion of the gastric cardia. The anastomosis was performed in the right thoracic cavity.

The postoperative course of this patient was smooth and uneventful. Fig. 19 shows a postoperative roentgenogram of the patient, the anastomosis being observed at the level of the aortic arch.

SUMMARY

There have been many varying techniques used for the approach and for the anastomosis when subtotal esophagectomy has been necessary in the radical surgical treatment of malignancy of the esophagus. However, the operative method which we have introduced in this report appears to us to be the best. This opinion is based on the fact that we have utilized a variety of methods in many esophageal operations in the past seven years, not a single one of them having proved satisfactory until this new approach was devised.

This operative method necessitates only one incision, the thoracoabdominal extending from the right thorax, although incisions of the costal angles may be utilized to get complete exposure of the esophagogastric canal. However, neither costectomy nor incision of the diaphragm is required. In addition, the operative technique has shortened the operative time because of the simplified procedure, and reduced the amount of bleeding throughout the entire operative procedure.

However, this operation is applicable only for those patients whose gastric blood supply is not dangerously interfered with by the mobilization. If cicatricial healing of the gastric ulcer on the lesser curvature is noticeable, or if it is seen that ligation of the arterial arches on the lesser curvature is essential to increase the scope of the operation, then esophagogastric anastomosis is to be preferred. Since we have obtained such satisfying and enlightening results in our examination of the gastric blood circulation and can thus determine which arteries may be safely ligated without jeopardizing the blood supply of the gastric wall, we feel that intrathoracic esophagogastric anastomosis can be performed without any fear.

In conclusion, subtotal esophagectomy can be performed with ease and assurance. Both this operation and resection of the esophagus and cardiac portion of the stomach for lesions of the lower esophagus can be performed from the left thoracoabdominal approach as easily as our predecessors were able to perform them over ten years ago.

It is my hope that this report will be of some benefit to surgeons who, now or presently, will have occasion to perform these operations.

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HUMAN MEASUREMENTS INVOLVED IN TRACHEOBRONCHIAL RESECTION AND RECONSTRUCTION PROCEDURES

Report of a Case of Bronchial Adenoma*

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IN THIS laboratory, problems related to tracheobronchial resection and reconstruction have been investigated.[1-4] Important phases of the experimental aspects of this problem have been concluded.

The clinical application of tracheobronchial resection and reconstruction would appear to be important in traumatic injuries of the bronchi and in tuberculosis. Such procedures for bronchogenic carcinoma would appear to have merit only in unusual circumstances. Most instances would fall into the group of palliative rather than curative operations for obvious reasons. Although tracheobronchial reconstructive procedures are applicable to the clinical entities listed previously, the work in this laboratory has been directed toward the problem of benign bronchial tumors.

TRACHEOBRONCHIAL MEASUREMENTS IN THE HUMAN BEING

In order to bridge the hiatus between the experimental facts and the clinical application of tracheobronchial reconstructive operations, certain additional anatomic knowledge is necessary. One bit of missing information relates to the spatial relationship of the tracheobronchial tree and the luminal diameters of bronchi which conceivably might be anastomosed to each other. In order for a theoretical plan of action to be meaningful, information relating to the following items is of importance: (1) the distance between the carina and the major bronchial take-offs; (2) the luminal diameters of various areas of the lower trachea and bronchi.

Consequently, 136 fresh human cadavers were studied at autopsy. The distances between the various take-offs of the bronchi and segments were measured. There were fifty-seven female cadavers with an age range of 13 to 86, the average age being 68 years, and seventy-nine male cadavers with an age range of 18 to 90, with an average age of 66 years. The measurements are schematically presented in Fig. 1.

In another group of fifty-five fresh human cadavers, measurements were made of the luminal diameters in various areas. There were thirty-three female cadavers with an age range of 13 to 86, the average age being 67 years and twenty-two male cadavers in an age range from 46 to 83, with an average age of 68 years. These measurements are presented in Fig. 2.

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**Trainee, National Cancer Institute.

In evaluating the luminal diameters, particularly of the lower bronchus, it should be pointed out that the measurements may seem greater than might be expected. This is due to the fact that in the area under question flattening of the bronchi occurs. The data were obtained by sagittal section of the bronchi with removal of the top half and measurement of the bottom portion in situ. Therefore, the measurement is accurate but the greatest diameter has been obtained of an ovoid sphere. If the lower bronchus were distended, undoubtedly the cross-sectional area would be smaller than a segment of the main bronchus with a comparable diameter as recorded.

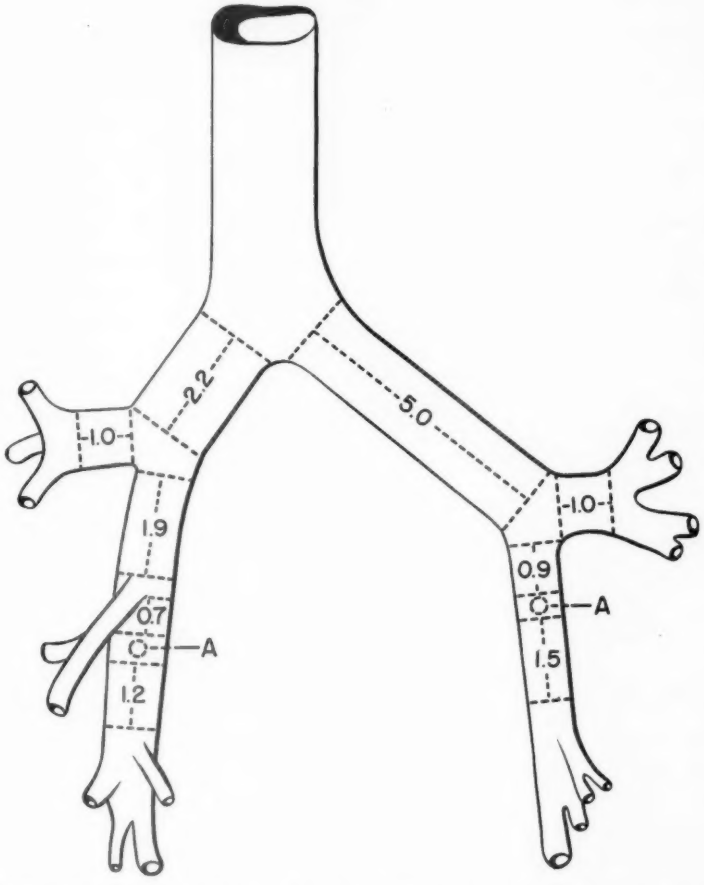


Fig. 1.—Average measurements in 136 fresh cadavers of the spatial relationship of the carina and bronchial tree. *A* indicates the orifice of the dorsal or superior segment of the lower lobes.

From human measurements, together with the experimental data in animals, it is possible to evolve various plans of excision and reconstruction dependent not only on the location of the tumor, but also on other important circumstances existent in each patient. It is apparent that if a peripheral adenoma were encountered, a lobectomy or segmental excision would be advisable.

In addition to tumor location and luminal and spatial relationships, further attention must be paid to the volume requirements of the preserved pulmonic

tissue. In "tailoring" the distal bronchus, care must be taken so that the spared lung lies comfortably in position with sufficient room to allow for its complete expansion.

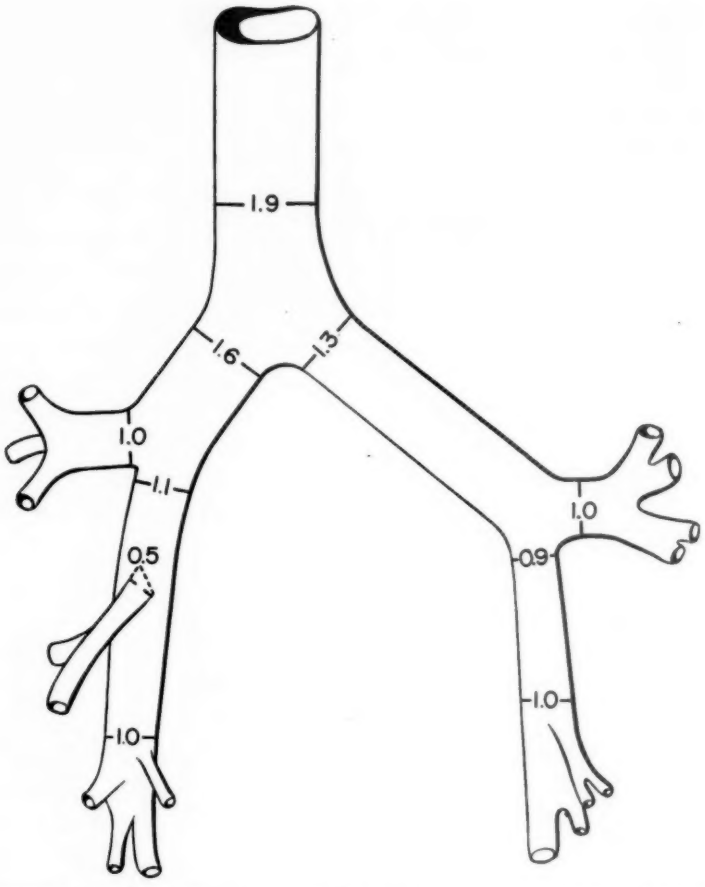


Fig. 2.—Average luminal diameters of the various areas which might be utilized for anastomotic procedures. These figures represent the averages in fifty-five fresh cadavers with the exception of the diameter of the lower lobe bronchus before it divides into the basal segments. This latter diameter represents the average measurement in twenty cadavers.

CLINICAL APPLICATION

Planned bronchial excision with reconstruction of the bronchial tree has been accomplished in patients with tuberculous stenosis by Gebauer.[5] He has shown the feasibility of the resection of a stenotic area on both right and left sides combined with a resection of either upper lobe and the anastomosis of the main bronchus on either side with the distal bronchus. Tuttle[6] in 1947 performed an unplanned reconstructive procedure similar to that to be reported in a patient with bronchiectasis who had been subjected to a left lower lobectomy some years before.

CASE REPORT

The patient, a 64-year-old white man, was admitted to the hospital for the first time on Nov. 27 1951, with a chief complaint of shortness of breath.

Approximately five weeks prior to admission he had developed an upper respiratory infection with blood-streaked sputum and pleuritic pain at the left posterior base. There was a twenty-pound weight loss.

Physical Examination.—The patient was thin and gaunt with a markedly emphysematous chest. Diaphragms were depressed bilaterally. There were decreased breath sounds, vocal sounds, and tactile fremitus at the left lateral base with some sticky inspiratory râles and an expiratory wheeze locally.

Except for a moderate leukocytosis, the laboratory findings were unremarkable.

X-ray examination of the chest on Nov. 28, 1951, revealed moderate pulmonary emphysema. In addition, a triangular area of moderate opacity in the posterior inferior portion of the left lower lobe was noted with some apparent infiltrative changes seen in this same area. It was felt that this was possibly due to atelectasis secondary to a bronchial lesion.

At bronchoscopic examination, Dec. 14, 1951, a granular appearing lesion was noted in the intermediate bronchus of the left lung approximately 1½ cm. distal to the left upper lobe take-off. This lesion appeared to be raised and to extend to or into the bifurcations of the left lower lobe. Microscopic diagnosis was possible carcinoma of the lung.

The patient was sent to the Cardiology Laboratory, where the following findings were noted:

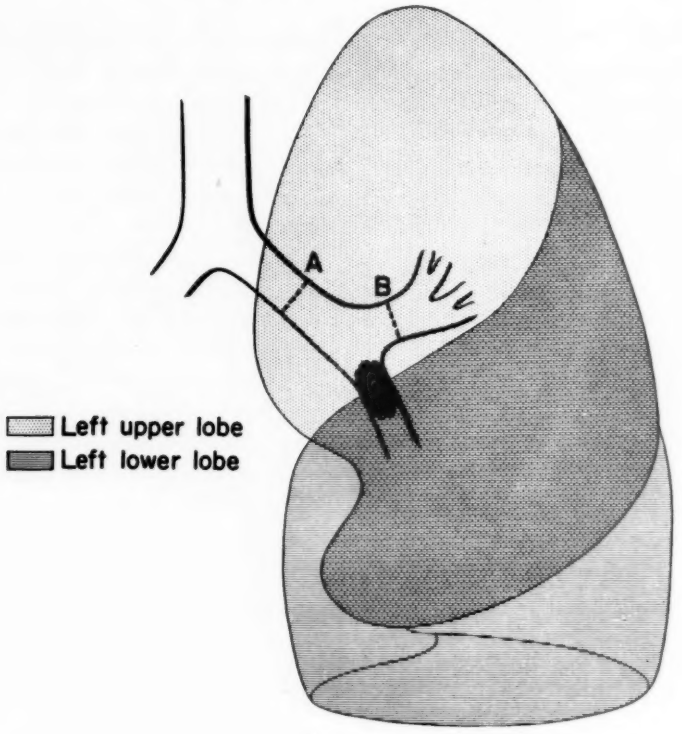
Vital capacity	3.25 L. in 4.9 seconds
Vital rate	0.67 L. per minute
Resting ventilation	17.0 L. per minute
Respiratory rate	20
Maximum breathing capacity	54.2 L. per minute (about one-third normal)
Respiratory reserve	69 per cent
Physical fitness index	11.3 (normal range, 13 to 16)

The consultant concluded that exploration could be attempted, but by all means the most limited excision possible should be performed.

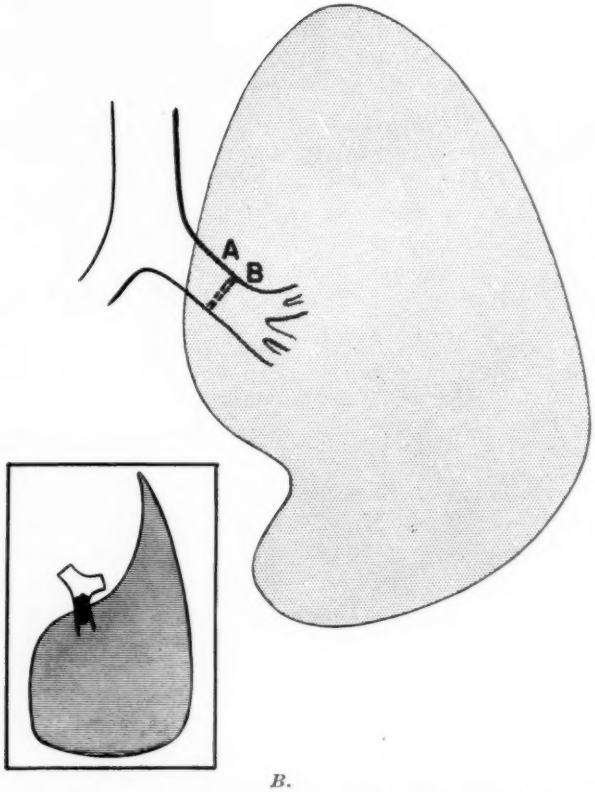
Operation.—A left exploratory thoracotomy was performed on Jan. 14, 1952. The operative procedure planned prior to surgery was carried out without event. A left lower lobectomy was performed with a portion of the left main bronchus and approximately 1 cm. of the left upper bronchus resected, en masse. The distal upper lobe bronchus was anastomosed by means of interrupted 0000 silk to the proximal left main bronchus, end to end. All blood supply to the upper lobe was preserved (Fig. 3).

The lung expanded well with positive pressure, and the left upper lobe realigned itself in the chest filling the pleural cavity considerably more satisfactorily than if a routine left lower lobectomy had been performed with the normal bronchial arrangement.

Postoperative Course.—The patient was able to cough up mucus fairly well. The highest temperature was 101.8° rectally, which occurred on the second postoperative day. At this time, the radial pulse was 120; respiration was 35. By the fourth postoperative day, the temperature and pulse were normal, although the respiratory rate was 25. On Jan. 19, 1952, the fifth postoperative day, the patient was dyspneic. A relatively large amount of mucus was aspirated, and the nasal oxygen catheter, which was plugged, was reopened, following which the patient was more comfortable. Some subcutaneous emphysema was noted over the left chest extending up to the neck. On Jan. 20, 1952, the subcutaneous emphysema was noted to have extended down the right arm, trunk, and medial aspect of both thighs. Physical examination revealed a collapsed left lung. A portable x-ray film of the chest confirmed this. There was a slight tracheal shift to the right. However, the patient was comfortable if the trachea was kept clean. The following day, Jan 21, 1952, the patient was much less dyspneic and the subcutaneous emphysema was noted to have receded. An x-ray film taken on Jan. 22, 1952, revealed the left upper lobe to be re-expanded. The anterior catheter was removed and the stitches were taken out. The patient was ambulated.



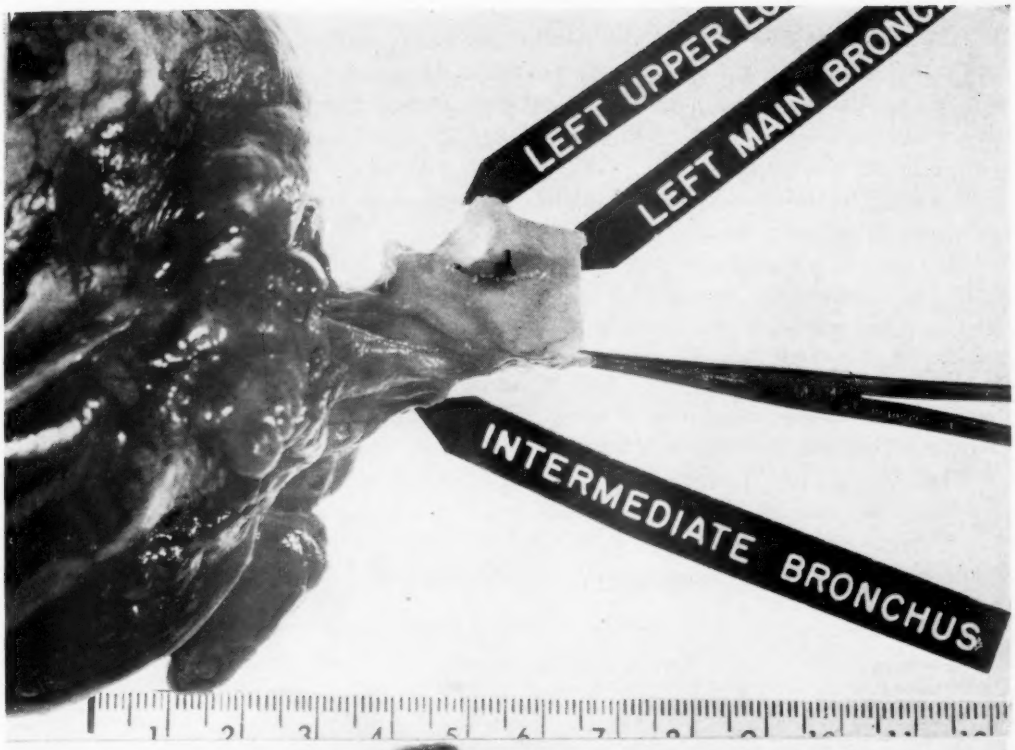
A.

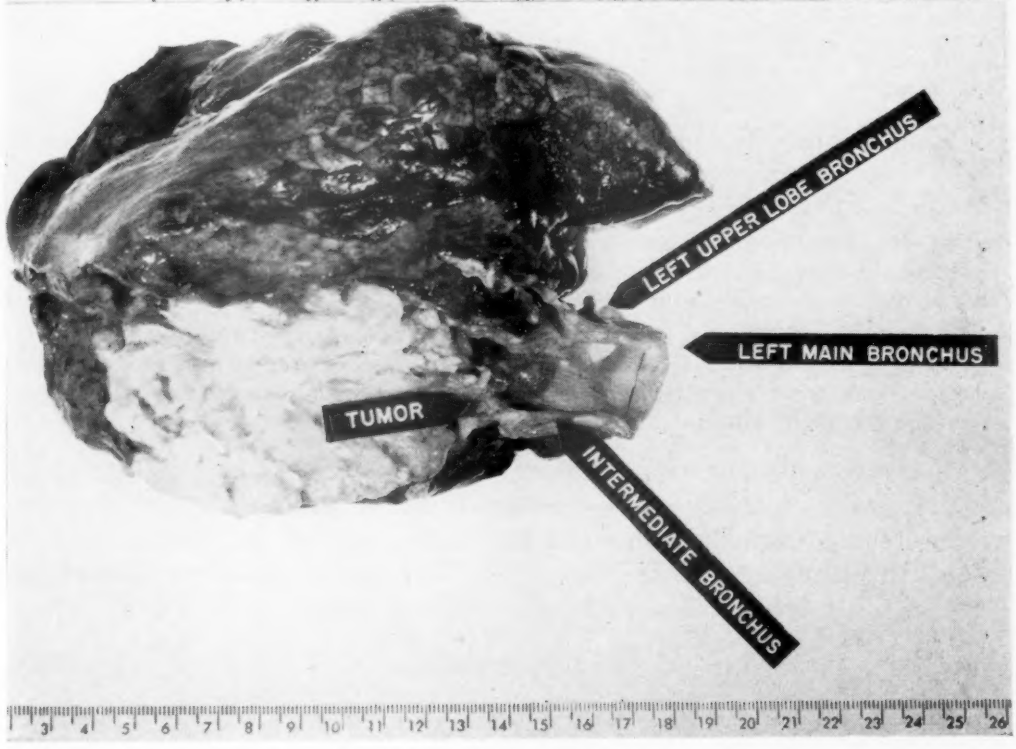


B.

Fig. 3.—*A*, This schematic drawing indicates the location of the bronchial adenoma. The lines *A* and *B* indicate the lines of transection. *B*, The reconstructive procedure is depicted. The inset sketch represents the component parts of the excised specimen.

A.





B.

Fig. 4.—Excised specimen. *A*, Close-up view of the proximal bronchial excision of the lower bronchus with the lower lobe, left upper, and distal left main bronchus. *B*, Opened view of lower lobe and tumor.

By the en masse excision of the structures indicated, an additional 4 cm. of the bronchus proximal to the tumor was excised than could have been removed with a lower lobectomy alone.

The microscopic report of the resected specimen was bronchial adenoma (doubtfully malignant) (Fig. 4).

He was discharged on the twenty-second postoperative day.

Progress Report.—Early following discharge, there was slight difficulty in raising sputum in the recumbent position. This, however, created no problem. An x-ray film taken on Feb. 26, 1952, revealed the left upper lobe to occupy comfortably the left half of the chest, and appeared normally aerated.

The patient was readmitted to the hospital on March 10, 1952, for bronchoscopy. A No. 7, 45 cm. bronchoscope was passed without difficulty. The right main-stem bronchus was normal. The carina was sharp and cords normal. The suture line in the left main bronchus was clear and without stenosis. The bronchus distal to the suture line continued in a straight line with the main-stem bronchus. For all practical purposes, one gained the impression that the scope was being passed into a normal left lower lobe. There was no evidence of recurrence. The distal bronchus was patent and appeared to function normally.

On June 25, 1952, bronchospirometry studies were carried out.*

Bronchospirometry

Barometric pressure, 755 Temperature, 22° C. Correction factor (S.T.P. 760 and 0°), 0.9193

Gas Exchange	*Normal Valves*	*Right Result*	*Per Cent*	*Left Result*	*Per Cent*	*Totals*
O_2 consumption (c.c./min.)	Dependent on BMR	199.0	62	121.0	38	320
Ventilation (L./min.)	5.0 L./min.	4.8	53	4.2	47	9
Ventilation equivalent	2.4-2.6	2.4		3.5		2.8
C.c. O_2/L. ventilation	42-45 c.c./min.	42.0		28.0		36
*Lung Volume**						
Vital capacity		1480	61	956	39	2703 2436

*In the normal person, 55 per cent of lung volume is on the right and 45 per cent on the left.

Summary.—There was 62 per cent oxygen consumption, right with 53 per cent ventilation on that side. On the left side, there was 38 per cent oxygen consumption with 47 per cent ventilation. Vital capacity studies with and without catheter checked within 267 c.c. It was felt that there was no block on either side.

The patient is alive and well without complaints at the present time, almost two years after surgery. The dyspnea is no longer a problem. He continues to be a somewhat garrulous individual, and he now states that he is able to talk continuously without stopping for breath, as was the case preoperatively.

Comment.—By resecting the lower lobe with portions of the left upper lobe and left main bronchus, approximately 4 cm. of additional bronchial tissue was removed proximally than could have been obtained by a lower lobectomy alone. In retrospect, an immediate tracheotomy following surgery would have lessened the problems associated with retained bronchial secretions.

SUMMARY

1. The average human measurements at autopsy of the tracheobronchial tree pertinent to the problem of resection and reconstruction have been presented.

2. A case of bronchial adenoma with the patient undergoing a bronchial resection with reconstruction has been presented. The respiratory function of

*Courtesy of Dr. Frank Cline, Jr., Firland Sanatorium.

the distal lung has been shown to be normal. To our knowledge, no other report has been made of a bronchial adenoma treated in this fashion.

3. We believe that bronchial resection and reconstruction is the operation of choice in selected cases of bronchial adenoma.

Acknowledgment.—We wish to acknowledge the assistance of Dr. Lloyd M. Nyhus, Dr. John W. Finley, Dr. Ralph J. Schlosser, and Dr. Donald G. Fletcher in obtaining at autopsy the measurements of the bronchial relationships.

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THE SYNDROME OF PERIPHERAL ARTERIAL INSUFFICIENCY WITH PARTIAL OCCLUSION OF THE ILIAC ARTERY

A Study of Nine Cases

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In 1940 Leriche[8] described a syndrome produced by obstruction of the terminal aorta and characterized by absent pulses in both lower limbs, sexual impotency, and an atypical intermittent claudication. Clinical and arteriographic studies since that time have shown that similar manifestations develop with partial obstruction of the common or external iliac arteries.

The syndrome due to partial occlusion of the iliac artery is one of intermittent claudication with a characteristic radiation of pain. With exercise, the pain begins in the calf and then may radiate to the thigh, hip, and buttock. The pain occurs in the presence of easily palpable peripheral pulses. A systolic bruit may be heard over the terminal aorta or iliac arteries.[13] Comparison of the femoral and the carotid pulses reveals that the femoral pulse is weaker and more easily obliterated by pressure. With exercise of the involved extremity there is disappearance of the pedal pulses and blanching of the foot and ankle. The blood pressure of the thigh is lower than that of the arm.

Sexual impotence, a characteristic finding in the Leriche syndrome,[9, 10] is uncommon in partial obstruction of the common iliac artery. Global atrophy of the lower limbs, also characteristic of the Leriche syndrome,[9, 10] is not found in partial iliac obstruction, although localized muscular atrophy may be present.

We have had occasion to study nine patients who met the clinical criteria of partial occlusion of the iliac artery. Six of these patients were studied before and after lumbar sympathectomy. The investigations included arteriography, reflex vasodilatation, plethysmography, oscillometry, ballistocardiography, and muscle clearance of radioiodine. The aims of the investigation were twofold: (1) to find, within the limits of readily available clinical and laboratory procedures, physiologic alterations which might serve to identify the syndrome and to differentiate it from the Leriche syndrome, and (2) to obtain information which might add to the understanding of certain aspects of vascular physiology.

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MATERIALS AND METHODS

To determine the anatomic site of the initial pain and its subsequent radiation, we had the patients walk at a rate of 120 steps per minute until pain occurred. Before and after exercise, the extremities were compared with respect to elevation pallor and dependent rubor.

Plethysmographic tracings and pulse recordings with gelatin tambour were made with the Burch Winsor Plethysmograph.[1] Records were obtained both with the patient at rest and following exercise to the point of pain. Arteriograms were obtained in all cases by direct injection of 35 or 70 per cent Diodrast into the aorta.[4]

Oscillometry was carried out before and after exercise with the Tycos Recording Oscillometer or with the Collens Oscillometer. The disappearance of pulses following exercise (jumping on one leg at the rate of two jumps per second), the appearance of pain in the calf, and the reappearance of pulses were carefully timed.

Muscle clearance was measured using the method first described by Kety[6] and later modified by Wisham and Yalow.[14] Approximately 10 microcuries of I^{131} buffered to pH 7.5 and in a constant volume of 0.25 ml. was injected through a 25 gauge 2½ inch needle into the gastrocnemius and quadriceps muscles of the involved leg. A lead shielded and collimated scintillation counter using a thallium activated sodium iodide crystal was placed over the injected area, and the counts per minute were continuously recorded by an Esterline Angus Recorder, which was driven by the relay of a Tracerlab Autoscaler. Approximately 5,000 counts were recorded for each plotted point, readings having been taken every two minutes for forty-five to sixty minutes.

The rate of disappearance of I^{131} was determined for approximately ten minutes, and then the subject exercised by hopping on one leg for 100 hops in from sixty to ninety seconds in the control group, or until severe pain appeared in the case of the patients (fewer than 100 hops). The subject was then placed in exactly the same position, and the remaining activity was recorded for approximately thirty minutes. A plot of the log of external counts per minute against time, corrected for the nonmoving clearance component, Figs. 7 and 8, yielded a line with negative slope, k. This may also be expressed as percentage of ion cleared per minute, K.

Ballistocardiograms were obtained in six cases.

Reflex vasodilatation tests were made after the method of Gibbon and Landis,[5] using an electric blanket as the stimulus to reflex heating rather than water at 43° to 45° C.

Unilateral or bilateral sympathetic blocks were performed in six cases.

RESULTS

Severe pain during minimal or moderate exercise in all cases began invariably in the calf and radiated to the ipsilateral thigh, hip, and buttock

TABLE I. CLINICAL SUMMARY

CASE	AGE (YR.)	LESION	CLAUDICATION	POTENCY	BRUIT	ELEVATION PALLOR		PULSE RETURN FOLLOWING EXERCISE (DORSALIS PEDIS)	BLOOD PRESSURE		ATROPHY OF CALF OR THIGH	BLANCHING DURING EXERCISE (FOOT)
						AT REST	FOLLOWING		ARM	LEG		
1. A. L.	54	Partial right common iliac occlusion	Calf to thigh to hip	+	+	0	+	5′ 0″	140/110	80/60	+	+
2. N. D.	47	Partial right common iliac occlusion	Calf only	+	+	0	+	2′ 15″	160/90	140/80	–	+
		Partial left common iliac occlusion	Calf only		+	0	+	2′ 0″	160/90	148/80	–	+
3. J. K.	47	Partial right common iliac occlusion	Calf to thigh to hip	+	+	0	+	2′ 0″	160/90	150/110	+	+
4. R. N.	57	Partial right common iliac occlusion	Calf to thigh to hip	0	+	0	+	3′ 20″	150/80	140/90	–	+
5. A. Y.	48	Partial left external iliac occlusion	Calf to thigh to hip	+	+	+	+	4′ 30″	140/90	70/0	+	+
6. J. H.	43	Partial right external iliac occlusion	Calf to thigh to back	+	0	0	+	4′ 30″	140/80	—	–	+
		Partial left external iliac occlusion	Calf to thigh to back			0	+	5′ 0″	—	—	–	+
7. W. W.	60	Partial right common iliac occlusion	Calf only	+	+	0	+	5′ 10″	160/90	140/70	–	+
8. L. H.	56	Partial left common iliac and external iliac occlusion	Calf only	+	+	0	+	6′ 10″	120/80	100/60	–	+
9. F. C.	34	Partial left iliac occlusion	Calf only	+	+	0	+	4′ 20″	140/90	100/60	+	+

(Table I). In no instance was the site of the original pain other than the calf. There was no elevation pallor at rest, but following exercise elevation pallor was found, and persisted for from one to three minutes. Blanching of the involved foot during exercise also occurred in all cases. The pedal pulses disappeared during exercise and did not reappear for two to six minutes following the cessation of exercise.

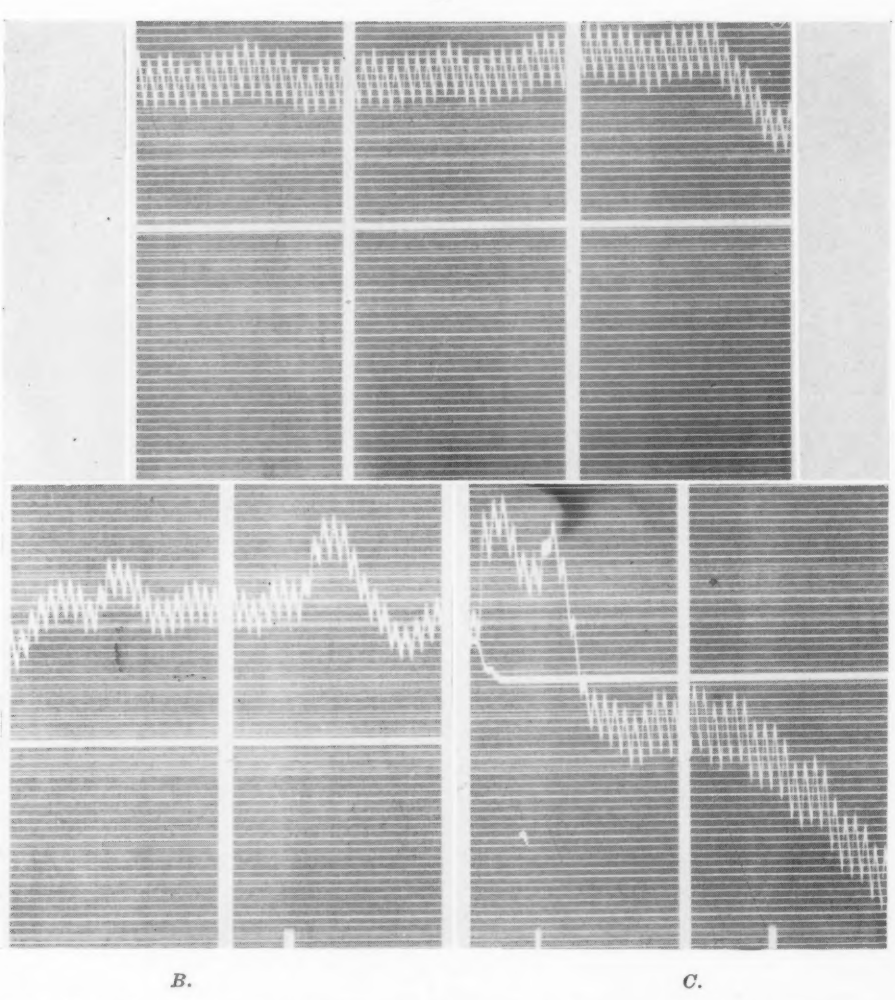

Fig. 1 (Case 2, N. D.).—Plethysmographic tracing, right second toe (postsympathectomy). *A*, At rest. *B*, Two minutes following exercise to claudication (eighty jumps on right leg at two jumps per second). *C*, Six minutes later, return to normal.

The plethysmograph (Fig. 1) and pulse tracings (Fig. 2) both demonstrated the decrease in pulse amplitude attendant upon exercise, and clearly indicated the time of return following exercise.

In all patients, a narrowing of the arterial lumen could be demonstrated by contrast roentgenography. Representative arteriograms are shown in Figs. 3 and 4.

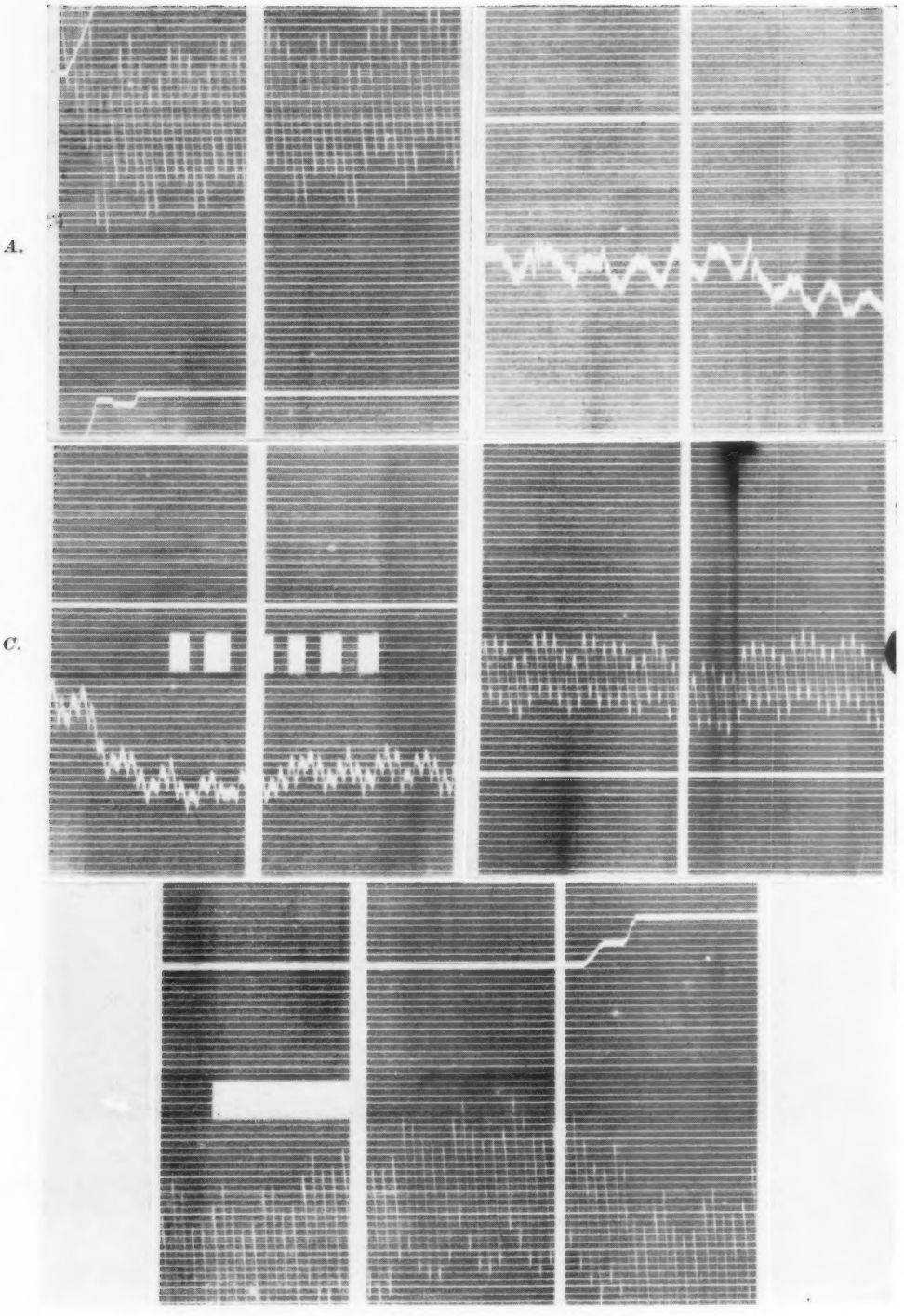

Fig. 2 (Case 2, N. D.).—Pulse tracing made with gelatin tambour over right dorsalis pedis artery (postsympathectomy). *A*, At rest. *B*, Thirty seconds following exercise to claudication (eighty-six jumps on right leg at two jumps per second). *C*, Five minutes following exercise. *D*, Ten minutes following exercise. *E*, Fifteen minutes after exercise. Interval marker indicates ten-second startle reaction (loud bell rung beside patient's head) with no response.

Fig. 3 (Case 3, J. K.).—Right common iliac artery, partial occlusion.

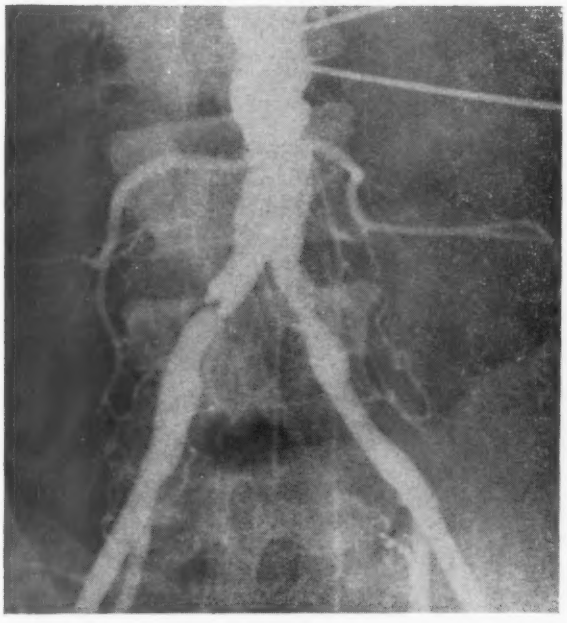

Fig. 4 (Case 2, N. D.).—Bilateral partial iliac occlusions.

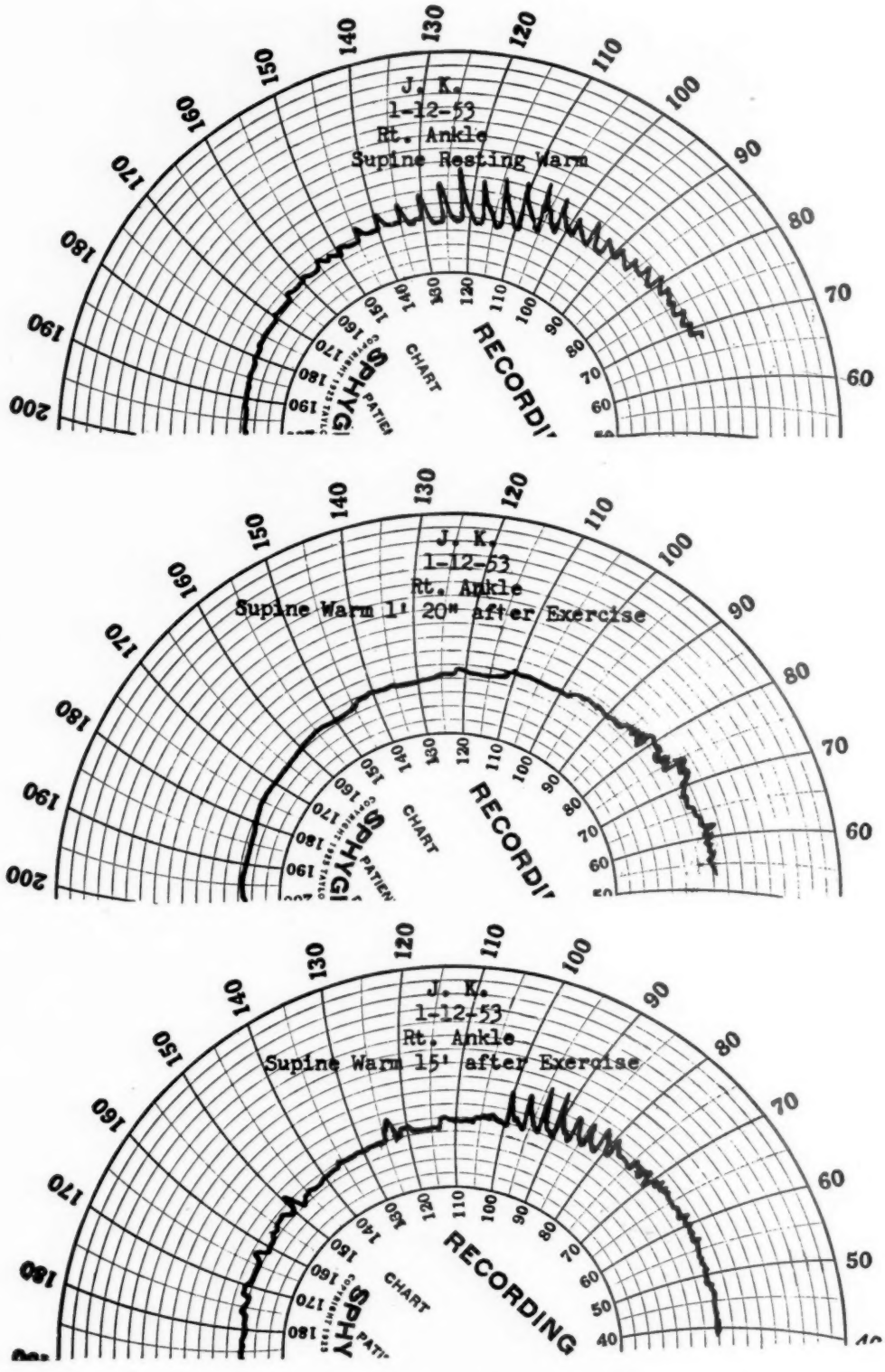

Fig. 5 (Case 3, J. K.).—Oscillometric tracing, right ankle, showing decrease in pulsations following exercise with incomplete return after fifteen minutes.

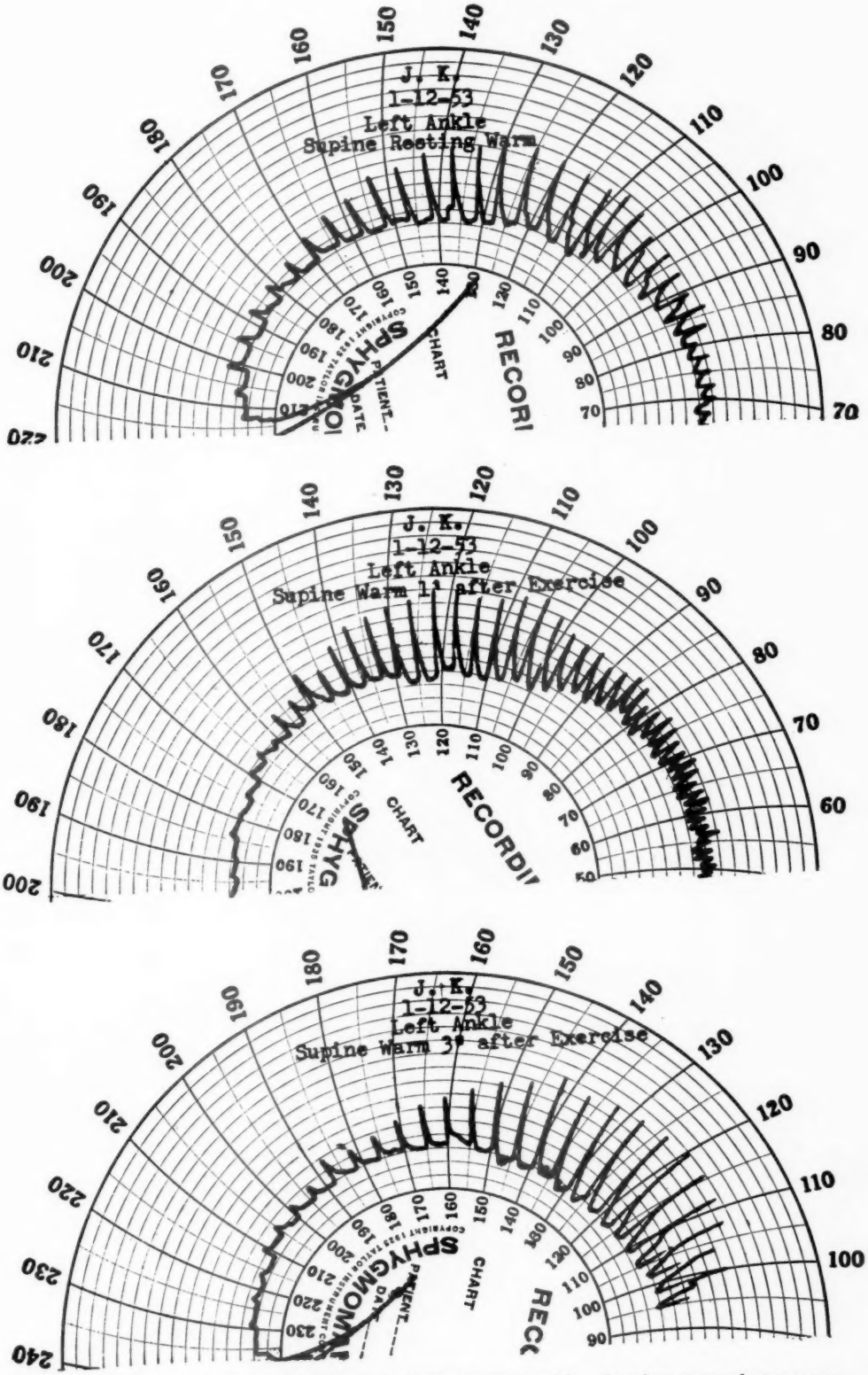

Fig. 6 (Case 3, J. K.).—Oscillometric tracing, left ankle, showing normal response.

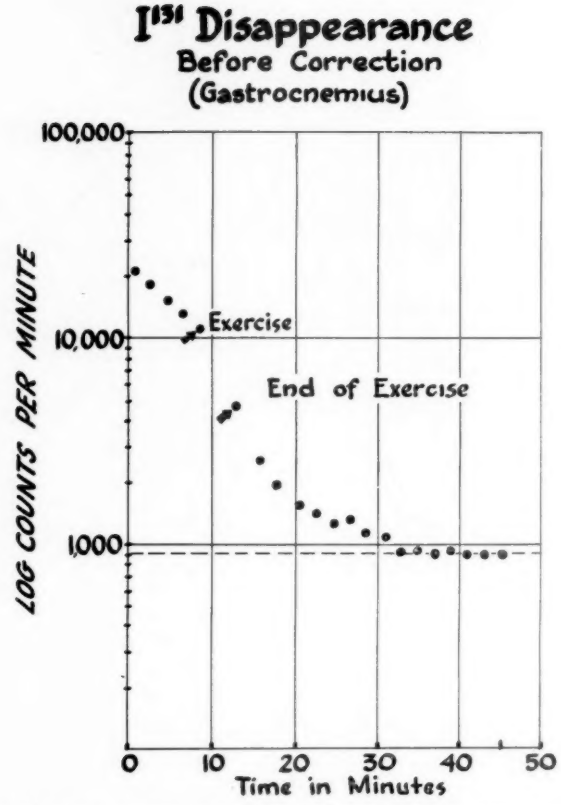

Fig. 7.—Graph showing variation of logarithm of counts per minute of I^{131} with time.

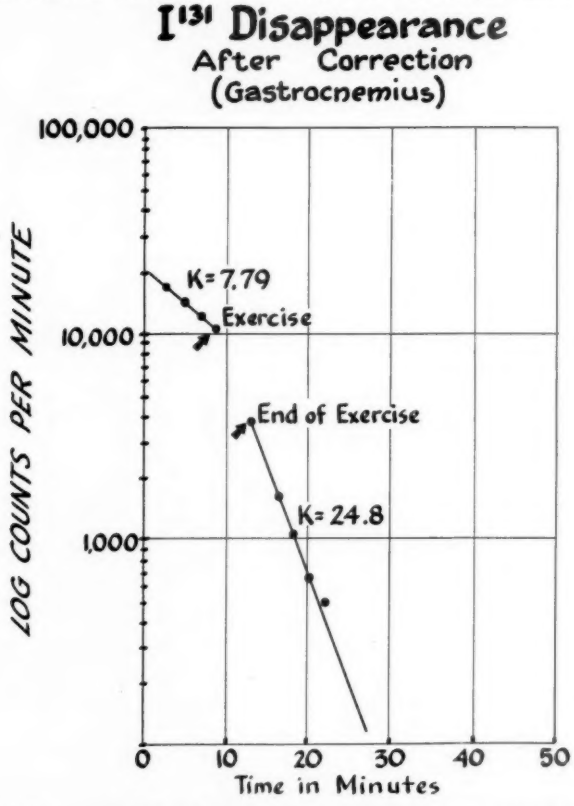

Fig. 8.—Graph showing variation of logarithm of counts per minute of I^{131} with time, corrected for nonmoving component.

Oscillograms of the calf showed a decrease in the oscillations following exercise, with the decrease persisting for over one minute in all nine cases (Fig. 5). The normal response following exercise, an increase of oscillations or a short decrease followed by an increase, is shown in Fig. 6.

Table II shows that there is no obvious difference in the percentage of I^{131} cleared per minute between resting control patients and those with intermittent claudication. Furthermore the rate of disappearance of the ion following exercise compared with the resting disappearance rate was approximately the same in the control and experimental groups.

TABLE II. PERCENTAGE OF I^{131} REMOVED PER MINUTE: $K = 100 \frac{\Delta N/N}{\Delta t}$

		K BEFORE EXERCISE	K FOLLOWING EXERCISE	$R = \frac{\text{AFTER EXERCISE}}{\text{BEFORE EXERCISE}}$
		Controls		
1-J.	Quadriceps;	3.46	5.55	1.60
	gastrocnemius	3.92	13.80	3.54
2-G.	Quadriceps;	4.75	8.78	1.93
	gastrocnemius	7.79	24.80	3.19
3-C.	Quadriceps;	9.00	24.70	2.75
	gastrocnemius	11.20	28.80	2.58
		Patients With Partial Iliac Artery Occlusion		
4-D.	Quadriceps;	2.31	7.3	3.16
	gastrocnemius	6.12	13.3	2.18
5-K.	Quadriceps;	14.40	14.4	1.00
	gastrocnemius	4.84	15.0	3.10
6-S.	Quadriceps;	4.72	11.5	2.44
	gastrocnemius	3.74	14.7	3.94

Ballistocardiograms on six patients were abnormal in each instance, but exhibited no characteristic pattern.

The vasodilatation tests were normal in all cases studied.

Following sympathetic block and lumbar sympathectomy in six patients there was no change in the clinical findings, response to exercise, oscillometry, plethysmography, or pulse tracings.

DISCUSSION

Each of the nine patients with partial occlusion of the common iliac artery had a characteristic intermittent claudication on exercise in the presence of easily palpable femoral and pedal pulses. This is in contrast to the situation found in the Leriche syndrome, where the pedal pulses are not palpable and the femoral pulse is not palpable or very feeble. In this group of patients, the blood pressure in the thigh was lower than in the arm, whereas in the Leriche syndrome, blood pressure is not obtainable in the thigh. Inability to maintain an erection is a characteristic finding in the Leriche syndrome (progressing to actual sexual impotence in long-standing cases),[9] but this finding of decreased sexual power was found in only two of the nine patients in this group. Localized muscular atrophy in the lower limbs with partial iliac artery occlusion may occur in contrast to global atrophy of both

lower extremities found in the Leriche syndrome. Elevation pallor was found in partial iliac obstruction only after exercise to the point of pain, whereas elevation pallor is present at rest in the patients with the Leriche syndrome.[9] In both syndromes a bruit may be heard over the terminal aorta or common iliac arteries.

Patients with the Leriche syndrome have an atypical intermittent claudication described as a feeling of extreme weakness or weariness in both lower limbs immediately on walking or while standing.[8, 9] If these patients are encouraged to walk to the point of appearance of actual pain, a "true" intermittent claudication will occur. The pain will, however, begin in the buttock and then radiate to the hip, thigh, and calf. This radiation of pain on exercise in the Leriche syndrome (and in total obstruction of the common external iliac artery) differs from that of partial iliac artery obstruction, where the pain begins in the calf and radiates successively to the thigh, hip, and buttock.

Two laboratory procedures are of importance in the differential diagnosis. The oscillogram shows no pulsations in the calf in the Leriche syndrome, but shows decreased or normal pulsation at rest in partial iliac obstruction. Following exercise, however, there is a decrease in the pulse in these patients rather than the increase found in the normal persons. This inverse relation of the oscillometric tracings was also found by Ejrup[2, 3] in his study of 660 cases of peripheral arterial obliterative disease. The arteriogram or aortogram actually demonstrates the lesion and represents the measure by which the definitive diagnosis is reached.

The ballistocardiogram, plethysmograph, reflex vasodilatation, and I^{131} clearances did not aid in the differential diagnosis.

Radioiodine clearances in these patients were made in an attempt to correlate the occurrence of pain with a decrease in clearance (representing blood flow). The fact that no decrease in clearance was found either before or after exercise may be correlated with the patients' experiencing no pain at those times, and with the pain of intermittent claudication ceasing almost immediately on termination of exercise. It would be of interest to measure muscle clearance during the actual period of exercise when the patient is experiencing pain.

The disappearance of the dorsalis pedis pulse during exercise where one was previously palpable points to either (1) a lack of sufficient blood to distend the peripheral artery or (2) vasoconstriction distally. Pearl[11] in 1937 described disappearance of the pulses in the extremities following exercise, which he attributed to a vasomotor phenomenon. Some of Pearl's patients, however, were later found to have an organic obstruction.[12]

Because thrombosis of the terminal aorta may begin as common iliac artery thrombosis, recognition of this syndrome followed by appropriate therapy may prevent or delay aortic thrombosis.[10] Accordingly, despite the failure of sympathetic block to alter the patient's symptomatology favorably,

lumbar sympathectomies were performed in six of the nine cases.[9, 10] There was no discernible effect on the symptoms, although the adequacy of sympathectomy was proved by the lack of a startle reaction during plethysmography and by the maintenance of digital temperatures five to ten degrees above a room temperature of 18° to 20° C. Specifically, sympathectomy did not affect the occurrence of pain during exercise, reappearance of pulses following exercise, oscillometry, or the plethysmographic or pulse tracings.

Kinmouth and associates[7] have shown in the rabbit and cat that there is little if any sympathetic control of the major arteries down to and including the femoral artery, and that change in caliber of these vessels followed blood pressure change only. It is our feeling that the syndrome presented here is attributable to changes occurring on an obstructive basis, and is not due to vasomotor effects mediated via the lumbar sympathetic nervous system.

CASE REPORT

J. K., a 37-year-old engineer, was admitted to the neurological service of the University of California Hospital on Feb. 15, 1952, with a chief complaint of severe right leg pain. Eight months prior to admission, the patient first noted onset of calf pain, which appeared after walking three or four blocks. When the patient continued to walk, this pain increased in severity, radiating to the thigh, hip, and buttock. This progressed until at the time of admission the pain appeared after the patient walked approximately one block. The patient stated that he had smoked approximately fifteen cigarettes a day for many years.

Physical examination revealed a well-developed, obese white man; blood pressure was 160/80, right arm. Pertinent physical findings included the following: (1) There were palpable pulsations of equal intensity in brachial, radial, and ulnar arteries bilaterally. (2) The femoral, dorsalis pedis, and posterior tibial pulses were all palpable bilaterally, but were markedly diminished on the right. (3) When compared with the right carotid artery, the right femoral pulse was more easily obliterated by pressure. (4) The feet were moist and cool, but there was no dependent rubor or elevation pallor. (5) There was a 2 to 3 cm. atrophy (circumference measurement) of the right thigh and calf when compared with the left. (6) Ophthalmologic examination showed the discs to be flat, of normal color, with the edges clear and well defined; retinal vessels were of normal caliber and distribution; no exudates or hemorrhages were seen. Laboratory tests revealed a negative serologic test for syphilis. Hemoglobin was 15.7 Gm. per 100 c.c. Serum cholesterol was 234 mg. per cent.

The following procedures were performed: (1) Exercise: When the patient hopped on the affected leg (right) at the rate of two hops per second, the right foot blanched immediately, pain appearing in the right calf at the end of thirty seconds. As the patient continued to hop, pain appeared in the right thigh at forty seconds and in the right buttock at forty-five seconds. At this point the patient was unable to exercise further. (2) Pulse recordings: Palpation of the pedal pulses was attempted at forty-five seconds, but no pulse could be found. The pedal pulses could not be palpated in the right foot until three and one-half minutes after cessation of exercise, while color returned to the foot approximately twenty seconds after completion of the exercise. Finally, with the patient at rest, oscillometric tracings revealed diminished pulse amplitude in the right calf and thigh as compared to the left. A reflex vasodilatation test revealed a normal response with a slight delay in the upper extremity and a normal rise of temperature to full levels of vasodilatation in the toes of both feet. Plethysmographic tracings revealed a decrease in amplitude of the pulse waves following exercise. This decrease persisted for one and one-half minutes. Also, pulse tracings of the dorsalis pedis

artery following exercise revealed a decrease in amplitude which did not return to normal for over seven minutes.

On Feb. 21, 1952, a direct puncture aortogram was carried out under general anesthesia. Six serial films were taken at approximately eight-second intervals. These revealed a constriction of the right common iliac at its take-off from the aorta. There was dilatation of the aorta for 3 to 4 cm. above its bifurcation. Arteriosclerotic changes on the lower abdominal aorta and left common iliac artery were also present.

Following conservative therapy, the patient was discharged from the hospital on Feb. 24, 1952.

On March 6, 1952, the patient was admitted to Franklin Hospital, and on March 7, 1952, a right lumbar sympathectomy was performed (first, second, and third lumbar ganglia). The postoperative course was uneventful, and the patient was discharged from the hospital on March 14, 1952. At that time, a reflex vasodilatation test showed maintenance of the temperature of the toes at 28° to 32° C. despite exposure to an environmental temperature of 19° C. Clinical examination following discharge from the hospital revealed little or no change in the clinical or laboratory findings described previously, with the exception that the right pedal pulses were more easily palpable at rest. On Dec. 23, 1952, the hopping test was repeated, and again revealed pain in the calf at thirty seconds and in the thigh at forty seconds. Palpation immediately following exercise revealed the pulses to be absent for over two minutes. Color did not return to the foot following exercise for approximately fifteen seconds. Measurement of the right thigh and calf still showed 2 to 3 cm. of atrophy.

Despite the appearance of pain during hopping at approximately the same time as before sympathectomy, the patient felt he could walk a greater distance without pain than before the operation. There were, however, no quantitative laboratory data to support the patient's statement.

SUMMARY

1. A syndrome due to partial obstruction of the common or external iliac artery was studied in nine patients.

2. The clinical and laboratory criteria for differentiating partial iliac artery obstruction from the Leriche syndrome are discussed.

3. Sympathectomy had no effect in six cases, indicating that the basis for the phenomena observed is obstructive rather than vasomotor in origin.

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BENIGN CYSTADENOMA OF PANCREAS

Report of Four Treated Cases, One by Whipple Type of Resection

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BENIGN cystadenoma of the pancreas is a rare lesion. Mozan[1] reviewed the literature in 1951 and concluded that only forty-nine definite cases, including one of his own, were reported in the literature. Since Mozan's report, Sawyer,[2] Tagariello,[3] and Haukohl[4] have recorded a total of four additional cases, making the total of reported definite cases fifty-three. Because of the apparent relative rareness of this lesion it was thought worth while to record four additional cases treated surgically and followed from two and one-half to ten and one-half years. One of these patients had a Whipple type resection of the head of the pancreas.

The report of Mozan[1] establishes the frequency of symptoms in patients with benign cystadenoma of the pancreas. In the case reports reviewed in his report, a palpable mass was present in 82 per cent of the patients, dyspepsia in 73 per cent, and pain in 57 per cent. When very large tumors were present, premature gastric satiation, gaseous distension, belching, nausea, and vomiting were the most frequent symptoms. Fourteen per cent of the patients had associated diabetes mellitus. Only the case reported by Mozan had jaundice and ascites. There were seven times as many female patients as male patients. Only thirty-one of the patients reviewed by him had been operated upon, and the apparent operative mortality was 26 per cent, with the fate of three patients unknown. Only twenty-two of the patients had complete surgical extirpation of the lesions.

Case 1.—The patient, F. W., was a 59-year-old white woman, who for four months had had intermittent cramplike pains of the lower abdomen. The pain occurred one hour after eating and lasted for two to three minutes. During this same period of four months she had noted indigestion, anorexia, belching, passage of excessive amounts of flatus, dizziness, and occasional nausea not related to the abdominal pains. For one month, swelling of the abdomen with retraction of the umbilicus had been noted. She had lost fifteen pounds in the four months of illness.

Other than progressive deafness, palpitation, and nervousness, the systemic review of her history was negative. Physical examination demonstrated a tender, firm, upper abdominal midline mass extending from the palpable liver edge to just below the umbilicus.

An x-ray study of the stomach and small intestine showed the existence of an epigastric soft tissue mass which displaced the antral portion of the stomach and the first portion of the duodenum downward (Fig. 1). The gall bladder was visualized by the

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Fig. 1.—Downward displacement of stomach shown by x-ray film in Case 1, F. W.

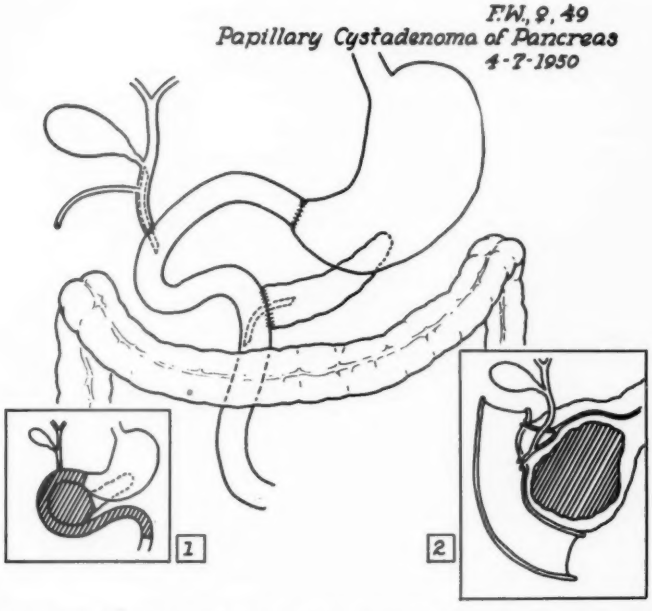

Fig. 2.—Diagrammatic representation of the reconstruction of stomach, jejunum, and remaining pancreas and common bile duct, Case 1, F. W. *1*, Insert showing the extent of the tissue removal. *2*, Insert showing the location of the lesion in the head of the pancreas.

Graham-Cole test, and was thought to be normal. There was no evidence of intrinsic abnormality of the stomach or duodenum. An electrocardiogram showed relatively early changes of the type which develop in the hypertensive state, the so-called left ventricular strain. A complete blood count and urinalysis were normal. The fasting blood sugar was 100 mg. per cent. The serum bilirubin level was 0.15 mg. in one minute and 0.53 mg. total. The prothrombin time was 74 per cent of normal.

Fig. 3.—Gross appearance of the sectioned lesion in relation to the duodenum in Case 1, F. W.

With a preoperative diagnosis of palpable carcinoma of the head of the pancreas, operation was performed (by H. A. Z.) on April 4, 1950. At operation the head of the pancreas was distorted, especially in the anterior-posterior plane, so that the head of the pancreas was a rounded mass approximately 8 cm. in diameter. Numerous large blood vessels coursed over the surface of the head of the pancreas. The common duct was not dilated. Several enlarged lymph nodes in the gastrocolic omentum were removed for biopsy. Frozen histologic sections of these lymph nodes were reported to show normal lymph node structure. A small portion of the stomach, the entire duodenum, the head of the pancreas, including all of the tumor, and the distal portion of the common duct were removed (Fig. 2). The proximal end of the jejunum was brought through the transverse mesocolon and anastomosed to the distal end of the stomach. Approximately eight inches below this anastomosis, a choledochojejunostomy was effected, and six inches below this the main pancreatic duct was anastomosed to jejunal mucous membrane. Through a separate opening in the common bile duct, a T tube was placed so that one limb of the tube protruded through the stoma into the jejunum. The entire operative procedure required four and one-half hours to complete. The cut surface of the gross original specimen is shown in Fig. 3. The postoperative course was uneventful. The patient's temperature was as high as 100.4° F. on only one occasion. She was discharged from the hospital on the twenty-first postoperative day.

Pathologic Report.—The specimen consisted of the head of the pancreas, which was largely replaced by a well-circumscribed, rounded, multiply loculated, cystic mass 5 cm. in diameter. Twenty-three centimeters of duodenum extended around one side of the pancreas. The duodenum and a portion of the common bile duct were loosely attached to the mass. The

surrounding pancreatic tissue, of whoch there was only a small amount remaining, appeared normal. A small portion of undilated, main pancreatic duct was seen. In section, the tumor was seen to be composed of a honeycombed mass of thin-walled cysts containing clear, watery fluid. Their size varied from 1 to 10 mm. in diameter.

The histologic sections (Fig. 4) showed the cysts to be lined by low cuboidal, uniform epithelial cells. In many areas, the lining wall became piled up, forming multiple papillary festoons. The pancreas surrounding the lesion appeared intact, with perhaps some increase in fibrous connective tissue around the larger ducts. A few islands of Langerhans were seen. The pancreatic lesion appeared to be more like a benign neoplasm than a congenital or a malignant disease. Diagnosis was papillary cystadenoma of pancreas.

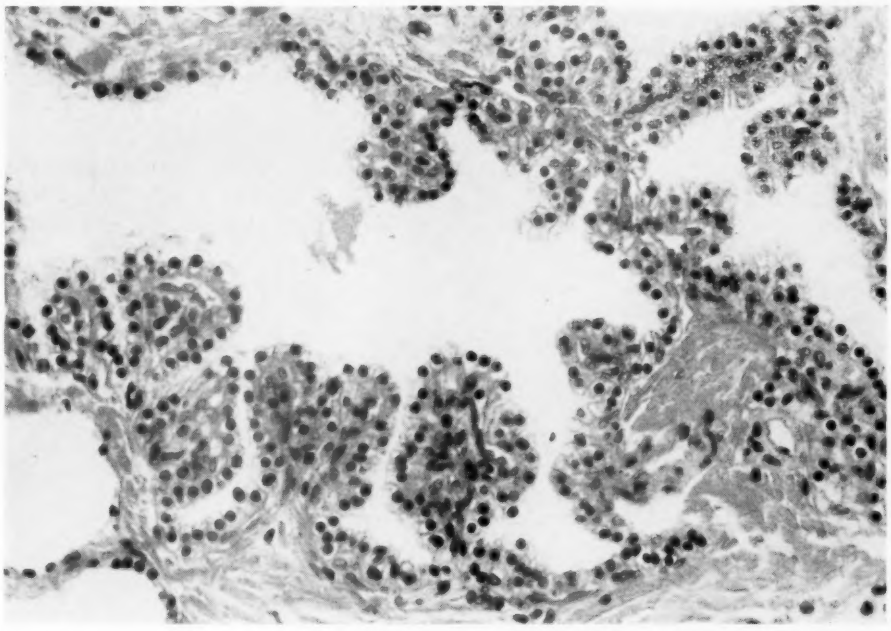

Fig. 4.—Photomicrograph, lesion of Case 1, F. W. (×200, reduced ⅓.)

During the first ten months following operation, on seven or eight occasions the patient had shaking chills, drenching sweats, nausea, and vomiting lasting four to six hours. Thereafter, she had jaundice and pruritis lasting approximately one week. It was apparent that she had intermittent hepatocholangitis. During this time she also frequently had indigestion, which she feels was partly the result of "nerves." During the last twenty-four months (of the thirty-four month period of postoperative observation), she had no recurrence of the jaundice, pruritis, or the other symptoms of which she had previously complained. She had gained eighteen pounds in weight. Her only complaints when last observed were excessive belching and the passage of excessive amounts of flatus.

Case 2.—The patient, S. Z., was a 40-year-old white woman, who was first admitted to the hospital Dec. 4, 1942. She gave a history of a more or less constant burning pain along the left costal margin and precordium. This pain was not related to food or exercise. The pain had been present for varying periods for the previous four years. More recently, pain tended to radiate to the right thigh and upper third of leg. One month before admission, a mass was discovered in the left upper quadrant by her family physician, who referred her to the hospital. The findings of note on this admission consisted of a firm, nontender, readily palpable mass in the left upper quadrant. The mass was freely movable and descended with respiration. Laboratory studies were essentially negative, except for a moderate anemia. X-ray examinations revealed an extrinsic mass displacing the

stomach to the right and anteriorly, and displacing the kidney downward. The patient was transferred to the surgical ward and operated upon (by J. E. R. and H. A. Z.) on Jan. 12, 1943. The gastrocolic omentum was divided to gain access to a large retroperitoneal cyst which was seen to arise from the tail of the pancreas. During efforts to remove the most posterior portion of the cyst, however, the cyst ruptured, and attempts to free this lowermost portion were unsuccessful. The cyst contents were therefore aspirated, and the free portions of the cyst were excised. A cigarette drain and a rubber tube drain were sewn into the remaining adherent portion of the cyst wall and exteriorized through a left stab wound. The cyst measured 11 cm. in diameter and its external surface was smooth. The internal surface was slimy, with numerous small areas of hemorrhage. There were several low ridges in the lining of the cavity and numerous bulbous papillary projections, which were soft, thin-walled, and cystic. Secondary cysts contained clear, mucoid material. Microscopic examination showed the cyst wall to be composed of a dense, fibrous, partly hyalinized connective tissue. The cyst wall was lined with an interrupted layer of tall columnar epithelium thrown into numerous folds (Fig. 5). Similar cells lined the papillary masses and secondary cysts. Occasionally these cells showed nucleoli compressed into a crescent in the base of the cell. In some, the cell surfaces were ruptured with the cytoplasmic contents bursting into the lumen of the cyst. Similarly lined acini were also present beneath the surface epithelium. The pathologic diagnosis made at this time was cystadenoma of the pancreas.

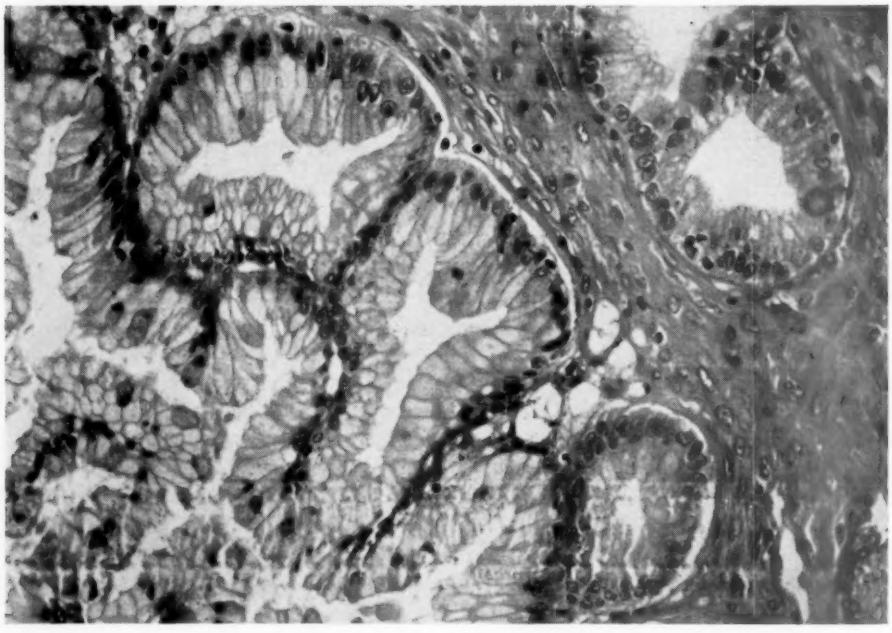

Fig. 5.—Photomicrograph, lesion of Case 2, S. Z. (×200, reduced ⅓.)

The patient's postoperative course was uneventful. It was decided to leave the rubber drain in place for an indefinite period. The patient was discharged on the nineteenth postoperative day. She was readmitted in the eleventh postoperative month for study and possible removal of the drain. X-ray studies at this time showed no connection of the fistulous tract to any viscus, and were otherwise negative except for slight displacement of a portion of jejunum to the right. The possibility of a recurrent pancreatic cyst was considered to explain this finding, but thought not likely. The drain was removed and the patient discharged, following which procedure the sinus closed. The patient was readmitted

to the hospital five years later. She had noticed tarry stools several weeks previously. Examination at this time again revealed a smooth firm mass, which was movable and palpable on deep inspiration, present in the left upper quadrant. Gastroscopy revealed deformity of the posterior wall of the stomach interpreted as probably due to extrinsic pressure. Laboratory studies revealed a strongly positive benzidine test for blood in the stool. Other laboratory studies were essentially negative. A second operation was performed Aug. 14, 1948 (by J. E. R.). At this time, a firm but cystic mass was present on the posterior wall of the greater curvature of the stomach. It was smooth and freely movable. Due to close adherence of the cyst wall to the surrounding structures, it was not possible to remove the cyst completely, and therefore the cyst was again marsupialized. The postoperative course was uneventful. Since the second operation the patient has been well and continues to gain weight. Ten and one-half years after the original operation she continues to have small amounts of discharge through the rubber drainage tube, which has been kept in place.

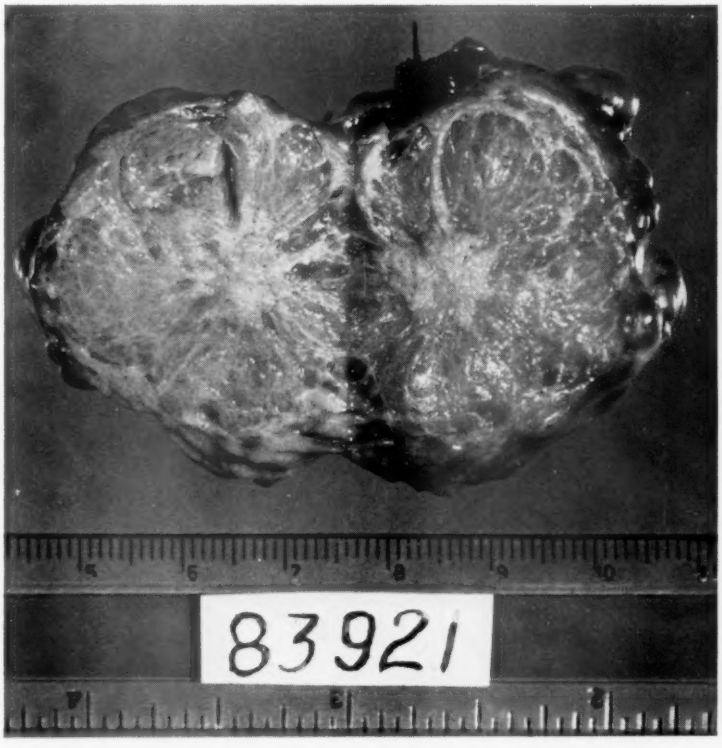

Fig. 6.—Gross appearance of sectioned lesion, Case 3, E. C.

CASE 3.—The patient, E. C., was a 42-year-old white woman who was admitted on Dec. 4, 1950, to the Hospital of the University of Pennsylvania on the Gynecologic Service of Dr. Franklin Payne. The patient's chief complaint was of metrorrhagia and dysmenorrhea. Her family physician had palpated a right adnexal mass.

The family history and past medical history were not contributory. Systemic review was negative with the exception of a mild upper respiratory infection one month previously. Physical examination revealed a somewhat tender, orange-sized mass just to the right of the umbilicus. This did not descend with respiration.

After a dilation and curettage of the uterus and cervical biopsy, the abdomen was opened through a subumbilical, midline incision. On exploration of the abdomen, an encapsulated, spherical mass 3.5 cm. by 3 cm. was found arising from the head of the pancreas. The external surface of the mass was studied with clear cysts about 6 mm. in

diameter. A frozen section was performed by Dr. Robert C. Horn. He made the diagnosis of a papillary cystadenoma of the pancreas. One of us (J. E. R.) excised the mass in toto with a surrounding cuff of normal pancreatic tissue. The gross cut specimen is shown in Fig 6. There was no evidence of spread of the tumor. A Penrose drain was placed in the bed of the pancreas and the wound closed. The drain was removed on the seventh postoperative day. The postoperative course was uneventful except for persistent clear discharge from the sinus tract remaining after removal of the drain. Grossly the tumor was well encapsulated. On section it was seen to be composed of myriads of small cysts separated by thin septa. Centrally there was a firm granular core of pale tissue 1 cm. in diameter resembling the center of an orange. Microscopic examination of the tumor confirmed the diagnosis of cystadenoma of the pancreas (Fig. 7). The lesion was composed of cystic spaces of irregular shape, which were lined by a layer of epithelial cells. These were for the most part cuboidal, but in numerous areas columnar and much vacuolated. Between the cysts were coarse septa of connective tissue. At the periphery, the lesion seemed to merge with pancreatic parenchyma. The surrounding pancreatic ducts were distended. The patient was discharged from the hospital on the eighteenth postoperative day. The drainage gradually diminished. When seen three months postoperatively, the patient was asymptomatic. The wound was completely healed. She has been symptom-free for the two and one-half years since operation.

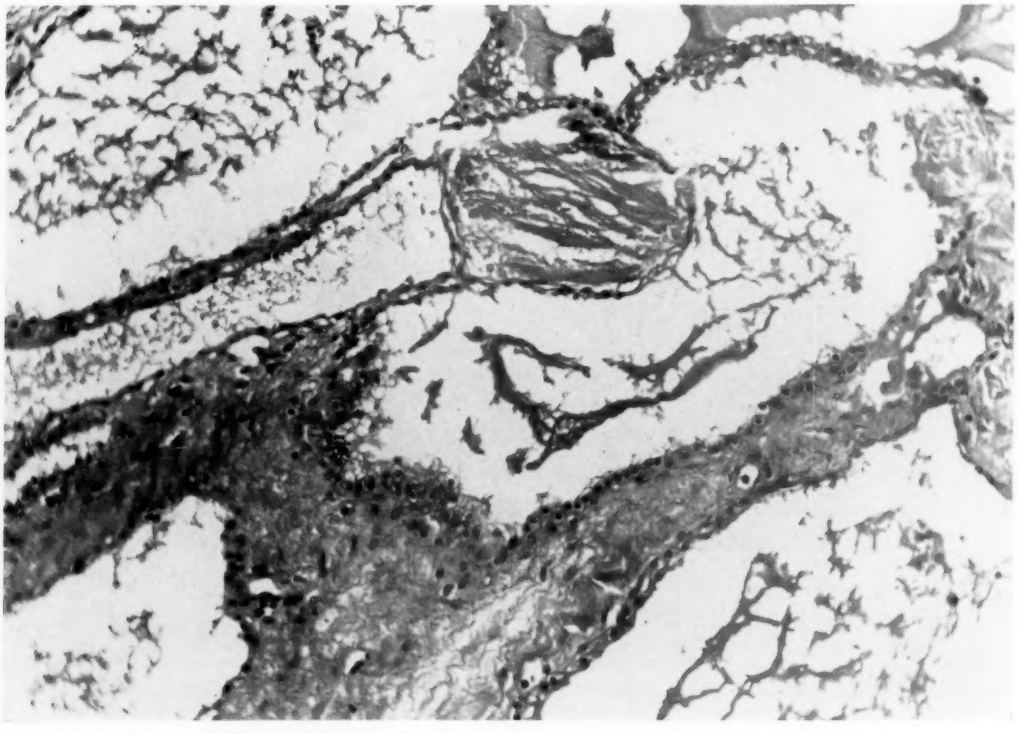

Fig. 7.—Photomicrograph, lesion of Case 3, E. C. (×200, reduced ¼.)

CASE 4.—D. D., a 47-year-old Negro woman, had chief complaints of pain and swelling beneath the left breast of six months' duration. She described the pain as being episodic and sharp in the right upper quadrant of the abdomen and with radiation toward the left axillary area. She had had "excessive" gas, flatulence, and vague abdominal discomfort for nearly one year. On physical examination a large hard mass was palpable in the left upper quadrant. It extended 7 cm. below the costal margin and from the

midline to the anterior axillary line. She had a hemoglobin level of 66 per cent and a lymphocytosis of 49 per cent. A gastrointestinal x-ray film showed the stomach to be displaced anteriorly and to the right by a soft tissue mass. The urogram showed the left kidney to be distorted, presumably by a kidney tumor. At laparotomy, March 10, 1949, a cystadenoma measuring 14 by 10 by 4 cm. was excised from the body of the pancreas. The tumor was a multiloculated cyst containing a watery mucinous fluid. On histologic examination a great deal of fibrosis and necrosis was evident. Ducts lined by cuboidal epithelium and groups of islet cells were seen. A few glandlike structures lined by columnar epithelium were present. Epithelium and cuboidal and columnar types lined the cystic spaces, which contained much debris. The epithelial nuclei were regular. There was no evidence of invasion of the stroma. The histologic diagnosis was cystadenoma of pancreas and hematoma of pancreas. The patient was entirely free of symptoms after operation and at the time of her last follow-up visit three years after operation.

DISCUSSION

Although it has been suggested that those lesions which show papillary projections on histologic section be regarded as malignant, the more common practice has been to consider such lesions benign, in the absence of direct evidence of malignancy.[2] The fact that three of the patients here reported had the papillary type of cystadenoma and have been followed for from two and one-half to ten and one-half years without evidence of metastasis would tend to justify the opinion that a diagnosis of malignancy is not justified on the basis of the finding of papillary projections. None of the patients reported here had evidences of jaundice or diabetes. It would appear that the most satisfactory type of treatment of benign cystadenoma of the pancreas is complete surgical extirpation whenever this can be safely accomplished. It is recognized that the patient reported in Case 1 might develop ulceration of the jejunum because the gastric juices are unneutralized in the first portion of the jejunum. Ordinarily we would prefer to have the common bile duct and pancreatic anastomoses proximal to the gastroenterostomy.

SUMMARY

Fifty-three cases of definite benign cystadenoma of the pancreas have previously been reported in the literature. The most common symptoms associated with this lesion, as described by Mozan, are given. The case reports of four female patients with benign cystadenoma of the pancreas treated by surgery are recorded. These patients are alive and well two and one-half to ten and one-half years after the operation. Photographs of the gross and histologic findings are included. Evidence is presented to support the view that histologic papillary projections alone do not indicate malignancy in cystadenoma of the pancreas.

ADDENDUM

Since this article was submitted for publication, the patient reported in Case 1 had several additional episodes of hepatocholangitis. At operation on Jan. 30, 1953, a stricture at the site of the previous choledochojejunostomy was found and repaired. A cholecystojejunostomy was also performed. Exploration of the abdomen revealed no evidence of recurrence of the cystadenoma. During the same hospital admission, a left radical mastectomy was performed for carcinoma of the breast. The patient was well when seen on Feb. 2, 1954.

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Case Reports

RECURRING MYXOMATOUS CUTANEOUS CYST

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MYXOMATOUS cutaneous cysts or so-called "synovial lesions of the skin" were originally described by Jones and Markins[2] in 1880. Succeeding cases, although usually presented to dermatologic societies, have received scant attention in the medical literature. Only some thirty cases have been reported. The scarcity of adequate description of this condition, together with the fact that these peculiar cysts are usually extirpated by surgeons who have the embarrassment of seeing them recur repeatedly, has prompted the following report.

CASE REPORT

A. P., a 44-year-old white woman, first noted a growth on the dorsoulnar side of the right middle finger, at the level of the distal interphalangeal joint in July, 1951. (See Fig. 1.) No history of trauma preceded the tumor, which gradually attained the size of a "pea." Thinking it to be a blister, she "pricked" it open several times, each time discharging a small amount of syrupy clear fluid, and each time developing a prompt recurrence in one to two weeks' time. In November, 1951, the lesion was surgically drained and again recurred in four weeks' time. Complete excision of the lesion in January, 1952, was followed by a recurrence six weeks later. The lesion, at first asymptomatic, became somewhat tender to touch after excision, although it never showed any signs of inflammation. Pressure failed to collapse the lesion, although the wearing of a tight bandage around it seemed to prevent its continued growth, according to the patient. X-ray films of the finger showed no connection to the underlying bone or joint.

The patient was submitted to radiation therapy, receiving a total dose of 1,000 r in three treatments on June 21, 1952, July 22, 1952, and Aug. 21, 1952, respectively. Within four weeks following the last treatment, the cyst began to shrink and the skin overlying it became shriveled. By December, 1952, the cyst had completely disappeared and has not recurred to date. (See Fig. 2.)

The case presented is typical of those reported in the literature.[2-8] The patients are usually women (75 per cent) in their forties (average age, 48 years) with a history varying from a few months to a few years.

The cyst occurs on the dorsal surface of the fingers (one of Gross' cases occurred on a toe), usually in close proximity to and a little to the side of the distal interphalangeal joint. They vary from 5 to 12 mm. in greatest diameter, although usually are about the size of a pea. They are smoothly rounded, thin-walled structures and often can be transilluminated. The color is that of normal skin, although if the wall is thin it may have a bluish cast or a vesicular appearance. The surrounding skin is normal in appearance, unless altered by

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superimposed secondary infection. Pressure does not reduce the size of the mass, for the cyst cavity does not communicate with a joint, bursa, or tendon sheath. Tenderness is usually mild or absent. The patients frequently state that they have pricked the cyst open on several occasions, believing it to be a vesicle. The fluid released is clear and colorless and has a syrupy consistency. In every instance, the individual was surprised to find that such drainage gave only temporary relief and was followed by recurrence in two to four weeks' time.

Fig. 1.—Myxomatous cutaneous cyst showing characteristic location and appearance.

Fig. 2.—Same patient four months after x-ray therapy (1,000 r).

Pathologically the condition represents a localized degeneration in the corium. The connective tissue in this area undergoes a myxomatous change, the collagen gradually disappears, and a basic staining mucoid material collects between the remaining fibroblasts. As the process continues, liquefaction occurs in the central portion of this myxomatous tissue, resulting in a cavity

filled with semifluid material. The cavity has no epithelial or endothelial lining, does not communicate with any subjacent structure, and shows no evidence of inflammatory change, nor is there appreciable pathology in surrounding blood vessels.

The etiology of this degenerative process has remained obscure. The various theories, which suggest that it is due to localized repeated trauma, vascular insufficiency, or degenerated connective tissue tumors, a variant of Heberden's nodes, or an outpocketing of a synovial membrane, remain unproved.

Electrocoagulation, fulguration, incision and drainage, curettage, chemical cauterization, freezing with carbon-dioxide snow, surgical excision, and amputation have all been tried alone or in combination in the treatment of myxomatous cutaneous cysts. Excluding amputation as an utterly needless procedure, recurrence was practically universal in two to three weeks following these forms of treatment. In several of the reported cases, recurrence occured as many as eight times.

By contrast, permanent disappearance of the cyst resulted when an adequate amount of radiation therapy was used. A cosmetically perfect result is obtained by this means, with no perceptible residuum or scarring. Jacox and Freedman[8] recommended a dose of 1,400 to 1,600 r (physical factors: 100 kv. constant potential, 4 Ma., 30 cm. focal skin distance, no added filtration, intensity, 120 r per minute, portal size as determined by the lesion), and in their series they saw no undesirable side effects and permanent regression of the cyst in four to six weeks.

SUMMARY AND CONCLUSIONS

A case is presented of an uncommon cutaneous condition, characterized by the formation of a small recurring myxomatous cyst of the skin of a finger or toe. The lesion is produced by a mucoid degeneration of the connective tissue of the corium, the cause of which is unknown. It is resistant to all surgical forms of therapy and recurs promptly when incised, excised, cauterized, or fulgurated. It responds best to radiation therapy, which usually effects a permanent cure.

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TOTAL TRANSPLANT OF THYROID GLAND USING VASCULAR ANASTOMOSES

Report of Successful Result in Chronic Tetany

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PARATHYROID gland transplant was accomplished experimentally[1] in 1929 (Cattell). In 1934, Stone[2] and his colleagues used an isotransplantation technique of thyroid and parathyroid tissue in ten cases. Two of these were successful. These authors introduced the tissue culture method[3] of preparing the graft for transplant. However, others are not convinced that this technique[4] helps the viability of the graft. The "free" transplant has been most successful. A transplant to the left axilla was successful in the symptomatic relief of a patient for at least six months.[5] Another technique was used in dogs[6] whereby the parathyroid gland was fragmented and injected into the jugular vein, these emboli being deposited in the pulmonary tissue. This parathyroid tissue remained in the lung parenchyma.

The present consensus[7, 8] is that a small transplant obtained by flawless technique and transplanted to an avascular area not subject to excessive trauma is most likely to remain viable and active.

The human parathyroid gland up to the age of 10 years contains the "chief" cell, which is the active secreting cell. It is most desirable, then, to obtain parathyroid tissue from a child for transplant to a patient who has tetany. Since, in such young and tiny tissue, the parathyroid glands could be easily injured, it was thought preferable to obtain such tissue as a portion of the intact thyroid gland. It was thought further that the blood vessels between gland and host could be anastomosed.

Because of the good result achieved by this method of transplant, its use is reported in a case of chronic tetany.

CASE REPORT

E. M., a 28-year-old white woman, was admitted to the Northern Division of the Albert Einstein Medical Center on Nov. 21, 1952, for the purpose of transplanting freshly procured thyroid gland tissue. She was blood type AB, Rh positive. Past history dated for over ten years to a thyroidectomy. Following this, it was noted that she was suffering from bilateral recurrent laryngeal nerve palsy, severe hypothyroidism, and severe hypoparathyroidism. Tetany had been progressively continuous. By November, 1952, it was necessary for this patient to take daily from 30 to 80 c.c. of calcium gluconate intravenously in order to overcome tetany. An attempt to transplant parathyroid tissue using the tissue culture technique in 1949 was unsuccessful.

On Nov. 21, 1952, she had a serum calcium of 8.8 mg. per cent. There were positive Chvostek and Trousseau signs, and the patient was very miserable psychologically. Table I, which lists the blood chemistries, indicates that when not taking calcium this patient had

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a serum calcium level of 5.2 mg. per cent. While on calcium therapy, the calcium rose to 8.8 mg. per cent. Ionizable calcium was always measured at normal levels.

TABLE I. BLOOD CHEMISTRY STUDIES

DATE	TOTAL CALCIUM (MG. PER CENT)	PHOSPHORUS (MG. PER CENT)	TOTAL PROTEINS (GM. PER CENT)	CHOLESTEROL (MG. PER CENT)	REMARKS
December, 1947	5.2		5.7		Tetany
August, 1948	5.7	6.4	6.9		Tetany
February, 1950	7.8	4.5			Tetany
November, 1952	8.8		6.0	130	Tetany
Nov. 21, 1952					Operation
Nov. 24, 1952	15.6	3.4			Tetany
Nov. 28, 1952	10.1		5.0		Tetany
Dec. 8, 1952	9.2	4.2	6.6		No tetany
Dec. 11, 1952	9.7	3.6	7.2		No tetany
Feb. 18, 1953	9.4	4.0	6.4	278	No tetany

The pediatric department of the Albert Einstein Medical Center had been alerted to the possibility of transplant in this case. On the morning of Nov. 21, 1952, a 3-week-old boy died following sudden decompression of a myelomeningocele. Within one hour after death, the body was brought to the operating room. Under aseptic precautions, the entire thyroid gland including its vascular pedicles was removed (Fig. 1). The vascular pedicles consisted of the middle thyroid vein and its attachment to the external jugular vein on each side, plus the superior thyroid artery attached to the external carotid and its continuation as the common carotid artery bilaterally. The carotid arteries (approximate diameter was 5 mm.) and the jugular veins (approximate diameter was 4 mm.) bilaterally were secured against bleeding from their branches. Polyethylene tubing was inserted. The gland was bathed in and perfused with Darrow's solution containing 1 mg. of heparin per cubic centimeter. The gland was less than 2 cm. in diameter. Its weight was estimated at 1.5 Gm.

Within two hours, the patient for whom the gland was intended was brought to the operating room. A skin incision was made one-half inch above and parallel to the left Poupart's ligament and extending up approximately three inches from the pubis. The subcutaneous tissue was dissected to expose two large veins and an artery. The patient's veins were approximately 4 mm. in diameter and the artery approximately 3 mm. in diameter. It is probable that these vessels were the superficial external pudendal vein and the superficial external epigastric artery and vein. The superficial external epigastric vein was cut, thus presenting medial and lateral ends.

The left carotid artery of the transplant was joined by end-to-side anastomosis to the superficial pudendal vein, using interrupted through-and-through sutures of fine silk. The left jugular vein was joined by end-to-end anastomosis to the lateral segment of the superficial epigastric vein, using interrupted sutures of fine silk (Fig. 2). Immediately after completion of this portion of the anastomosis, the color of the transplanted gland changed from pale yellow to reddish purple. The right jugular vein was joined by end-to-end anastomosis to the medial segment of the superficial epigastric vein. The right carotid artery was anastomosed by end-to-end anastomosis to the available artery. Each anastomosis was inspected and leakage controlled by tiny pieces of Gelfoam. The artery-to-artery anastomosis was not completely satisfactory because of disparity in size and the partial obstruction to flow presented by the inversion of the wall of the larger vessel. However, blood did flow through it. The skin was closed with interrupted sutures of fine Dermalon.

The donor had died at 8:15 A.M.; operation for removal of transplant began at 9:15 A.M.; the procedure of vascular anastomosis and reimplantation was completed at 2:30 P.M.

Following the transplant, the patient's requirement for intravenous calcium remained almost unchanged for eight days. It was still necessary to use intravenous calcium gluconate

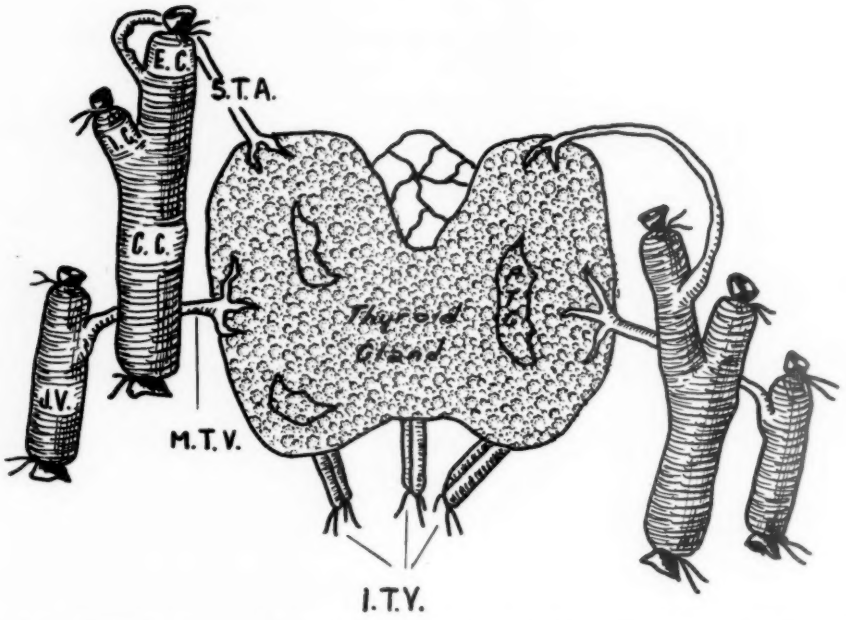

Fig. 1.—Drawing of thyroid gland and vascular pedicles removed from infant. *J.V.*, Jugular vein; *M.T.V.*, middle thyroid vein; *I.T.V.*, inferior thyroid veins and thyroid ima; *S.T.A.*, superior thyroid artery; *E.C.*, external carotid artery; *I.C.*, internal carotid artery; *C.C.*, common carotid artery.

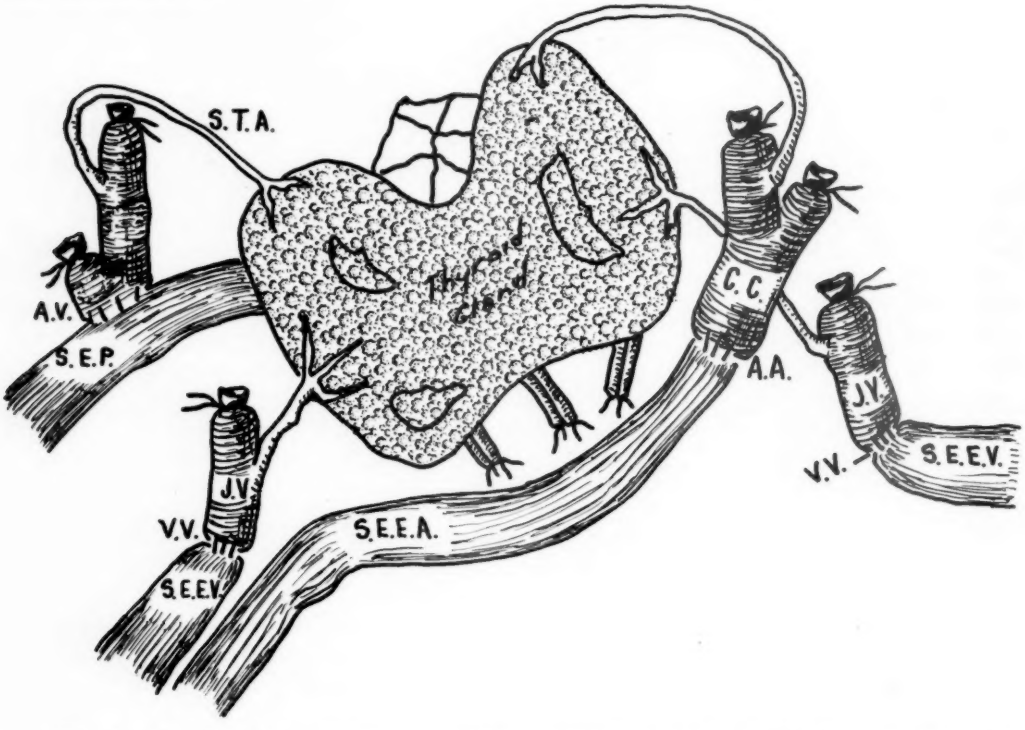

Fig. 2.—Drawing of anastomoses: vascular pedicles of gland and patient's vessels. *A.V.*, End-to-side anastomosis, comomn carotid artery to superficial external pudendal vein; *S.E.P.*, superficial external pudendal vein; *S.T.A.*, superior thyroid artery; *V.V.*, end-to-end anastomosis, internal jugular vein to superficial external epigastric vein; *J.V.*, jugular vein; *S.E.E.V.*, superficial external epigastric vein; *A.A.*, end-to-end anastomosis, common carotid artery to superficial external epigastric artery; *S.E.E.A.*, superficial external epigastric artery; *C.C.*, common carotid artery.

in doses of 20 to 40 c.c. once or twice daily. This was not readily understood. Finally, it was found that the patient's total blood protein had dropped from a level of 6.0 Gm. per cent four days prior to hospital admission to a level of 5.0 Gm. per cent. As soon as the blood protein level was brought to within normal limits by intravenous plasma and forced protein feedings, no further medication was needed. The patient had been taking small amounts of calcium and 2 c.c. of viosterol by mouth daily during the interval immediately postoperatively when she was still requiring calcium gluconate for relief of tetany. All medication was stopped on Dec. 11, 1952, except oral calcium, which was stopped on Jan. 6, 1953.*

Isotope (I^{131}) uptake was determined on the eighth postoperative day. It was found that the transplanted gland behaved as normal thyroid tissue (9 per cent uptake).

Since operation, the patient had normal menstrual periods, has had multiple teeth extractions, and has sustained other stresses with no ill effect. She has returned to normal activities. Previous signs of calcium deficiency have disappeared. The incision in the left groin healed; the site of the graft had been slightly indurated for one week, but there was no evidence that the tissue had become cystic, abscessed, or necrotic.

Re-evaluation was made Feb. 18, 1953. This was three months after operation, nearly eleven weeks after the last intravenous injection of calcium gluconate, and over one month after any medication whatsoever had been given. A.T. 10 and thyroid extract had been discontinued at operation in November, 1952.

There are complaints of coldness in the extremities, and the patient, when under emotional stress, notes occasional fleeting cramps in the calves and fingers. These subside spontaneously. She is able to complete her day's waitress duties. The only major complaints are backache and frequency, with occasional dysuria. It is felt that slight residual deformity from fracture of the thoracic spine (1948) and a chronic pyelonephritis are the causative factors. On occasion, the patient feels dyspneic and notes periodic ankle edema.

At present, temperature, pulse, respiration, and blood pressure are normal. Weight is 135 pounds (no change in three months). There is no edema, dyspnea, pallor, cyanosis, or tremor. Chvostek and Trousseau signs are not elicited. Skin and hair are of normal texture. The outlines of the transplanted gland are still palpable and the pulsations in the area are still present.

Complete blood count is normal. Blood calcium (9.4 mg.), phosphorus (4.0 mg.), and protein (6.2 Gm. per cent) are within normal limits (Table I). Pyuria is present. Sulkowitch test shows a faint trace of urinary calcium. Determination of radioactive iodine uptake now (6.2 per cent) reveals the presence of functioning thyroid tissue at the site of the transplant. Rate of basal metabolism on March 5, 1953, was reported at −9 per cent. The serum cholesterol is 280 mg. per cent.

DISCUSSION

Fortunately, in this case the patient's blood type is AB (Rh positive), thus permitting the transplant of tissue from a donor of any blood type. The transplantation in accordance with the method reported in this case is very tedious and exacting. Technically, it was possible to place only four or five sutures in end-on fashion to anastomose the vessels. These anastomoses were functioning when they were completed. It cannot be stated unequivocally that these are still patent. That the glandular tissue has functioned satisfactorily for three months can be inferred from the patient's clinical status and freedom from symptoms of hypothyroidism and hypoparathyroidism.

As indicated by Peer and Walker[10] in accordance with Roux's law, highly specialized tissue such as a secreting gland can continue to survive provided there is functional stimulation. Their study also demonstrated that cells can

*At the advice of Dr. Abraham Cantarow.[9]

stay alive for four days at body temperature if the grafts are merely humid. In addition, they demonstrated that the vascular system in free grafts tends to survive transplantation. They alluded to the skin, but it is felt that any effort made to assure the circulation of blood to new tissue will assist in the maintenance of viability for a longer time. As Cantarow[9] and others have indicated, only a few cells are needed in order to maintain the parathyroid function in the body.

It is understood that the follow-up interval since transplant is a short one. Nonetheless, there is sufficient evidence to indicate that the procedure was successful in that symptoms of hypothyroidism and hypoparathyroidism were relieved. The patient may be on the verge of myxedema at this time, since the cholesterol is high normal at 278 mg. per cent. It was never expected that the thyroid tissue would continue to function, so that the evidence, three months later, by tracer study that the transplanted tissue retained iodine was, indeed, surprising. Further observations on this patient will be forthcoming.*

SUMMARY

The case is reported of a 28-year-old woman who had suffered severe tetany of ten years' duration due to surgical trauma. This tetany was relieved by transplant of thyroid and parathyroid glands using vascular anastomoses. The gland was procured from an infant of 25 days.

In such critical glandular deficiencies as in the reported case, the utilization of very young thyroid and parathyroid tissue is efficient. It is suggested that the carotid and jugular vessels be anastomosed with the host's vessels to provide the gland with some nutrition until local circulation is adequate.

We express appreciation for their cooperation to the pediatrician (Dr. G. Elson) and to the parents of the child from whom the gland was obtained.

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*The patient, fifteen months following transplantation, is well.

MUCOCELE OF INVERTED APPENDICEAL STUMP FOLLOWING APPENDECTOMY

Report of a Case

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ALTHOUGH mucoceles of the vermiform appendix have been described since early in the nineteenth century, we have been unable to find recorded in the literature a case of mucocele occurring in the wall of the cecum at the site of a ligated and inverted appendiceal stump. The following is a report of such a case.

CASE REPORT

The patient was a white man, aged 58 years, who was admitted to the Indianapolis Veterans Hospital in October, 1952, complaining of right lower abdominal pain present for almost four years following an appendectomy performed elsewhere. The pain was described as being a continuous dull ache, not related in any way to eating. The patient had had nausea and vomiting prior to the appendectomy, but not since that time. There had been no hematemesis, melena, or change in bowel habits, and he had lost no weight. Physical examination was negative except for deep tenderness in the right lower quadrant of the abdomen. No masses were palpable. Blood count was normal and urinalysis negative. A gastrointestinal series revealed no abnormality, and cholecystograms showed good visualization of the gall bladder. Films of the barium enema revealed a smooth deformity of the inferior medial border of the cecum with a suggestion of a pressure defect on the terminal ileum (Fig. 1).

Records obtained from the previous hospital admission indicated that the appendectomy had been performed as an interval procedure, with an operative diagnosis of an old perforated appendix. The operative note stated that the base of the appendix was ligated with chromic catgut and inverted into the cecum with several interrupted silk sutures. Films following a barium enema two months after the appendectomy had been interpreted as normal. The patient's abdominal pain began shortly after this barium enema.

Because of the persistence of pain and the constant finding of a cecal deformity following barium enema, an exploratory laparotomy was thought to be indicated. It was performed on Oct. 21 after preparation of the large bowel with neomycin. When the abdomen was opened through a transverse incision, a firm smooth mass was palpated in the cecum. There was no gross evidence of tumor extending through the cecal wall or involving structures adjacent to the bowel. Therefore, the cecum was opened and the mass found to be submucosal with no evidence of growth through the mucosa. The mucous membrane was incised, and grayish jellylike material was found within the tumor. Several silk sutures were noted on the external surface of the cecum, presumably at the site of inversion of the appendiceal stump. Resection of the cecum was necessary in order to remove the entire mass. The terminal ileum was transected and an end-to-side ileocolostomy performed. The patient was discharged after two weeks without symptoms and with normal bowel function. Films of a barium enema, prior to discharge, revealed only the deformity created by removal of the cecum.

Pathologic examination of the resected specimen showed the cecal wall to be markedly thickened with increase in the amount of connective and muscular tissue. Large amounts of

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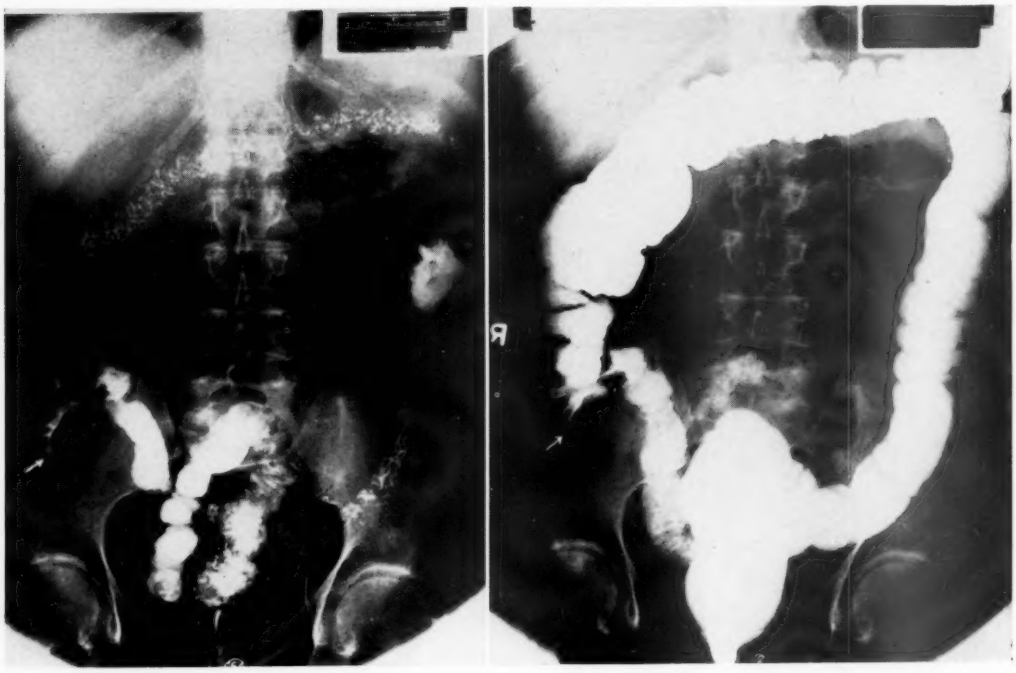
mucous material, occurring in lakes of considerable size, were seen. Fibrosis and occasional groups of normal mucous-secreting cells were found. The nuclei of the mucous-secreting cells did not appear neoplastic. A mild lymphocytic inflammatory reaction was present. Chemical examination of the mucoid material indicated that it contained true mucin with a complex carbohydrate component. The diagnosis was mucocele of the cecum, postappendectomy.

DISCUSSION

There is some difference of opinion in the literature concerning the first description of a mucocele of the appendix. Some authors[2, 6, 7, 9] credited Virchow with the first report in 1863, while others[2, 10] stated that Rokitansky first described the condition in 1842. All agreed, however, that Fere in 1877 first applied the term mucocele to describe a dilation of the appendix containing mucous material.



A. *B.*

Fig. 1.—Films of the barium enema showing smooth, constant deformity of the cecum.

Three conditions have been mentioned as necessary to produce a mucocele of the appendix. These include stenosis of the lumen of the appendix, continuous secretion of mucin, and an absence of virulent infection. Grodinsky and Rubnitz[7] found that mucoceles could be produced experimentally in rabbits by washing out the lumen of the appendix and completely ligating the organ. There is also some mention made of the importance of an intact blood supply to the appendix, at least in the production of experimental mucocele.[1]

Grossly, mucoceles vary greatly in size. They may be only several centimeters in length or may be as large as the 30 cm. specimen reported by Kelly.[12] Usually the dilated cyst contains a yellowish to gray colored jellylike material.

This contains pseudomucin and has also been known to contain true mucin.[2] Mucicarmine and safranine stains may demonstrate the presence of pseudomucin.[2] Certain chemical tests may demonstrate true mucin, as was possible in our case. Microscopic examination of a mucocele may show hyperplastic mucosa, although atrophy usually occurs as the cystic dilation increases. The involved wall may be replaced with fibrous tissue containing spaces filled with mucous material.[7]

The usual symptoms of an appendiceal mucocele are vague and not at all diagnostic.[3, 4, 6, 7, 9] Abdominal pain, usually in the right lower abdomen, and present for some time, is often noted. Occasionally, a mass may be palpated in the abdomen.[6, 9] Barium enema examinations may reveal a pressure defect in the cecum. Gastrointestinal symptoms, such as nausea, vomiting, change of bowel habits, and so forth, are usually absent.

The prognosis for mucocele of the appendix uncomplicated by pseudomyxoma peritonaei is excellent if the lesion is completely removed.[1, 3, 7] Bowel resection, as in this case, sometimes is necessary to assure complete removal.

Although the mucocele in our case occurred in the cecal wall at the site of an inverted appendiceal stump, rather than in the appendix itself, the symptomatology and pathologic findings were similar to those of mucocele of the appendix. The vague right lower abdominal pain and the pressure defect on barium enema were present, and constituted, in fact, the reasons for exploratory laparotomy. Other significant symptoms were absent. The history of previous appendectomy in our case made a correct preoperative diagnosis even more unlikely than in the usual case of mucocele. The pathologic picture of the removed specimen was similar to that described for mucocele of the appendix. The three factors previously mentioned as being necessary for the development of a mucocele also seem to have been present in this case. Yeager[13] has pointed out that the usual inversion of an appendiceal stump after ligation is not an inversion at all, but actually is simply the burying of the stump in a small blind pouch created by the inverting suture. A closed space is thus formed. If mucous-secreting cells should remain in the buried stump of the appendix, a mucocele might conceivably develop. Why such a condition occurs so rarely is unknown, although there are several possible explanations. The absence of blood supply to the crushed and tightly ligated stump may cause its intraluminal sloughing. Furthermore, if an absorbable material is used for ligation, its resorption may obviate the persistence of a blind pouch.

The possibility that our patient had originally a mucocele which was incompletely removed was considered unlikely, since the patient's hospital record indicated clearly that the appendix was small, the only abnormalities being adhesions and evidence of previous perforation.

SUMMARY

A case is reported of a mucocele present in an inverted and ligated appendiceal stump four years after appendectomy. The symptomatology and pathology of mucocele of the appendix is discussed briefly in relation to the reported case.

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ASCARIASIS OF THE COMMON BILE DUCT

Report of a Case Causing Symptoms After Cholecystectomy

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ASCARIS lumbricoides, the common roundworm, is believed to be the most common parasite found in man.[4, 5, 8] Reports of instances of ascaris infestations of surgical significance are found infrequently in the literature. Complications associated with this disease include intestinal obstruction due to a bolus of entangled ascarides,[2, 7] acute pancreatitis due to obstruction of the duct of Wirsung,[4] bowel perforation, obstructive appendicitis,[7] cholelithiasis caused by a nidus of ascarides,[1] obstruction of the common bile duct,[4] ascending cholangiohepatitis, and multiple liver abscesses.[2, 3]

We wish to present a case of choledochal ascariasis which was characterized by symptoms of biliary tract disease. The symptoms occurred three years after cholecystectomy, and the cause of the complaint was not discovered until after surgical exploration and T-tube drainage of the common duct. The unusual nature of this case lies in the fact that the worm, undiscovered at operation, presented itself at the cutaneous opening of the T tube on the twelfth postoperative day. As far as we can determine, this is the first case demonstrating this peculiar sequence of events to be reported in the literature.

CASE REPORT

A 40-year-old, 220-pound white woman was first admitted to the Los Angeles County Harbor General Hospital in July, 1950, complaining of right upper abdominal pain of fourteen hours' duration. She presented a twenty-five year history of symptoms suggestive of gall bladder disease for which a cholecystectomy had been performed at another institution in 1947. Following this operation, the patient was purportedly asymptomatic until January, 1950. From this date and during the succeeding six months prior to admission, she suffered at least nine attacks characterized by pain in the right upper abdomen radiating to the right infrascapular area and accompanied by nausea and vomiting. These episodes lasted from twenty-four to forty-eight hours and were increasing in degree of severity and duration. Jaundice, biliuria, and acholic stools were not observed with these attacks. The past history and systemic review were not contributory except as indicated in the present illness. The patient was born and raised in Nebraska, and for the fourteen years prior to the first admission had resided in California. On admission, the patient's temperature was 101° F. The positive physical findings were limited to the abdomen. The patient was markedly obese. Healed right subcostal and right lower rectus incisions were noted. The right upper abdominal quadrant was tender on deep palpation, but no masses, guarding, or rigidity was present. The white blood cell count was 11,700 with 64 per cent neutrophils and 13 per cent nonsegmented forms. No eosinophils were seen on this examination. The serum amylase and urinary diastase were reported to be within normal limits. The urinalysis was not contributory. A flat film of the abdomen revealed no abnormality. The patient's symptoms

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subsided under conservative management, and she was discharged after thirteen days to be followed in the outpatient department.

The patient was admitted to the hospital for the second time on Aug. 24, 1950, with essentially the same complaints and findings, and was discharged thirteen days later after a similar course of treatment. The provisional diagnosis at this time was possible calculus of the common bile duct or mild relapsing pancreatitis. An upper gastrointestinal roentgenographic study performed in the outpatient department was noncontributory. A double-dose oral cholecystogram revealed no gall bladder shadow. One month later, the patient was admitted for the third time under similar circumstances and after four days was discharged on a low caloric diet in preparation for a proposed common duct exploration if the symptoms recurred.

We had no occasion to see her again until June, 1951, when she sought admission for right upper abdominal pain of three days' duration. The physical findings were essentially the same as noted on previous admissions. When the symptoms had subsided, she was subjected to abdominal exploration. No abnormalities other than a surgically absent gall bladder and numerous upper abdominal adhesions were noted. The common bile duct was normal in size and consistency, and on supraduodenal exploration a No. 8 Bakes dilator passed with ease through the papilla of Vater without revealing any obstruction. A No. 18 T tube was inserted into the common duct, and a cholangiogram was performed at the operating table. The films confirmed the clinical impression and disclosed a normal extra- and intrahepatic biliary tree.

The patient's subsequent course was uneventful until the twelfth postoperative day, at which time the apparent cause of the prolonged complaint, a roundworm (Ascaris lumbricoides), presented itself at the open cutaneous end of the T tube and was extracted by an attending physician. It measured 17.5 cm. in length. After a course of hexylresorcinol, the patient was discharged from the hospital with the T tube in place.

She was admitted for the fifth time on July 11, 1951, because of difficulty in maintaining adequate drainage from the T tube. Ascaris ova were identified in the biliary drainage, but were not found in the stools. A second course of hexylresorcinol was administered. One month after operation, a follow-up cholangiogram was found to be negative. The T tube was inadvertently removed by the patient on the sixty-second postoperative day. The fistula closed spontaneously, and the patient has remained asymptomatic to date. The stools have remained free of ascaris ova.

SUMMARY

A case of Ascaris lumbricoides infestation of the common bile duct which caused symptoms of biliary tract disease three years after cholecystectomy is reported. The diagnosis was consistently missed, even after surgical exploration of the common bile duct and operative cholangiography, until the worm presented itself at the open cutaneous end of the T tube on the twelfth postoperative day.

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ADENOCARCINOMA OF THE ESOPHAGUS

Report of a Case of Glandular Metaplasia of the Esophageal Mucosa

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WE WISH to report a case of adenocarcinoma occurring in the lower end of the esophagus, distinctly separated from the stomach by uninvolved esophagus, and originating from glandular epithelium which lined the esophagus from the esophagogastric junction to at least the level of the aortic arch.

True adenocarcinoma of the esophagus is rare, and the number of reported cases is in sharp contrast to the oft-quoted incidence of this lesion. Most observers conclude that adenocarcinoma in the esophagus represents an extension from a gastric carcinoma.[3, 4, 8] Ackerman and Regato[1] agreed with this concept and doubted that adenocarcinoma of the esophagus constitutes an entity. Hewlett,[7] writing in 1900, reported that he had collected from available literature six cases of adenocarcinoma of the esophagus, four located in the upper two-thirds, and two located just above but separate from the stomach.[7] Feldman[6] in 1939 reported an esophageal polyp at the level of the sternal notch which proved to be an adenocarcinoma. In the same year, Carrie[5] reported an adenocarcinoma of the upper half of the esophagus which he believed had originated from a patch or island of ectopic gastric epithelium. He believed that this was the second authentic esophageal adenocarcinoma to be found in the literature, and called attention to Feldman's report.

CASE REPORT

F. C., a 66-year-old white, single, male farmer, was first admitted to the Minneapolis Veterans Hospital on Feb. 24, 1953. He had enjoyed good health until four months before admission, when he experienced dysphagia to solid foods. The dysphagia progressed until he was able to swallow only liquids. One month before admission he sought relief from his physician. Roentgenologic and esophagoscopic examinations revealed an ulcer of the esophagus. The symptoms continued, and he was admitted to this hospital. A sixteen-pound weight loss had been noted. There was no family history of cancer. Physical examination was negative except for evidence of recent weight loss. Laboratory examinations were within normal limits. There was no anemia. Roentgenologic examination of the esophagus revealed a sharp filling defect in the lower third of the esophagus with normal esophagus between the lesion and the stomach (Fig. 1). The esophagoscopist noted no mucosal abnormalities above the level of the lesion. During this latter procedure, inadvertent perforation of the distal end of the esophagus occurred. The patient experienced immediate severe epigastric and substernal pain, and the procedure was terminated. The patient was taken to the operating room immediately. Transthoracic exploration of the distal esophagus revealed evidence of perforation and a mass 2 cm. in diameter involving the esophagus but not fixed to any adjoining structures. The lesion was discrete, and between its lower border and the esophagogastric junction there was 5 cm. of apparently normal esophagus. The stomach was normal. The esophagus was resected from 8 cm. proximal to the lesion to just below the cardiac orifice.

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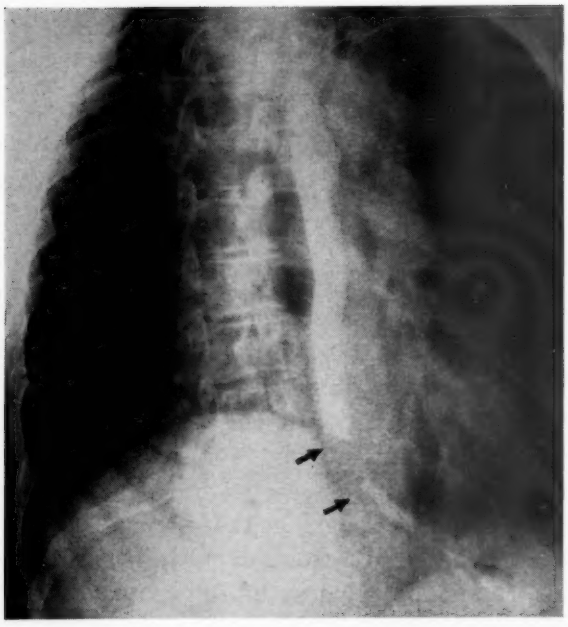


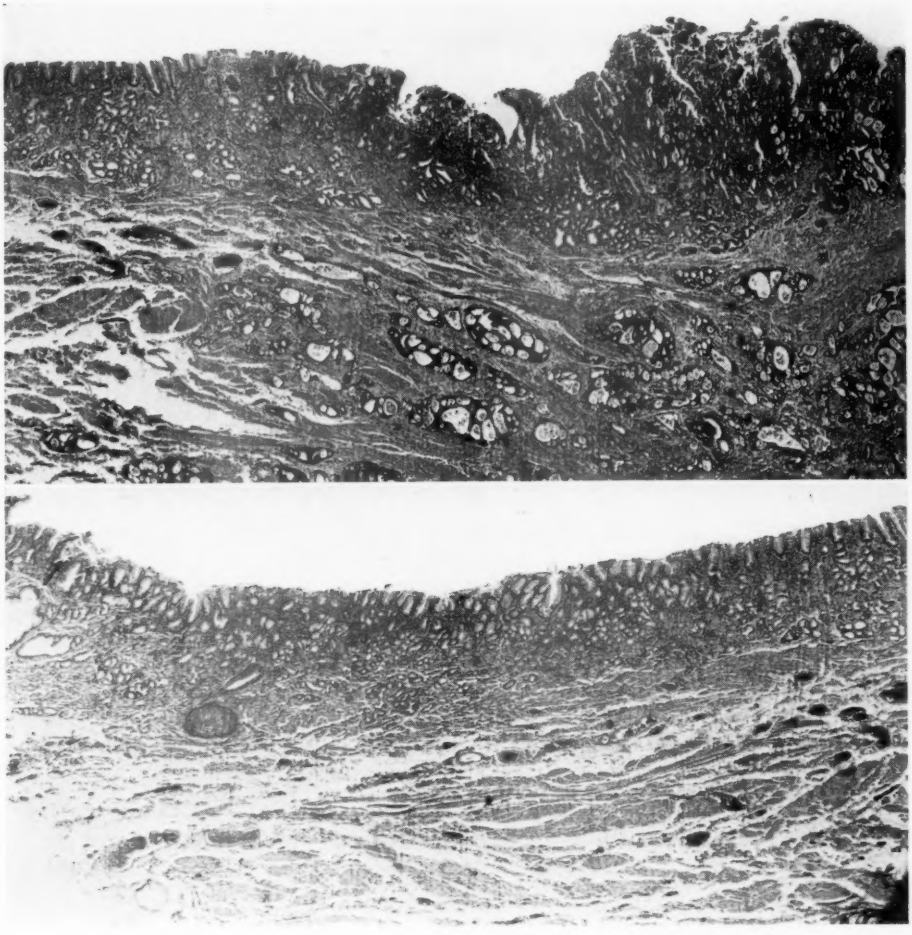
Fig. 1*A*.—Right anterior oblique roentgenogram after barium swallow illustrating sharp filling defect in lower esophagus with a normal esophageal mucosal pattern between the lesion and the gastric cardia.

Fig. 1*B*.—Spot film as in Fig. 1*A*.

An anastomosis was made between the fundus of the stomach and the proximal esophagus just below the aortic arch. The patient's immediate postoperative course was uneventful.

Pathologist's Description of the Resected Specimen.—The resected specimen included the distal portion of the esophagus and a small portion of the cardiac end of the stomach, and measured 10 cm. in length. In the mid-portion of the resected esophagus, a hard mass 3 cm. in diameter was found. Approximately 3 cm. of uninvolved esophagus was measured both proximal and distal to the tumor. Except in the area of the tumor, the mucosa appeared normal to gross inspection.

A.



B.

Fig. 2.—*A*, Section through the distal edge of the tumor illustrating the well-differentiated adenocarcinoma infiltrating the muscular layers of the esophagus. On the left side is seen the benign glandular epithelium lining the esophagus distal to the lesion. (Photomicrograph, × 24; reduced ⅓.)

B, Section through the proximal end of the resected esophagus (just below the aortic arch). The esophagus is lined by columnar epithelium compatible with the gastric cardia. No squamous epithelium was found. (Photomicrograph × 24; reduced ⅓.)

Microscopic sections through the tumor revealed a well-differentiated adenocarcinoma which was invading the muscularis mucosae. Clumps of tumor were also seen in lymphatic channels (Fig. 2, *A*). The esophageal mucosa distal to the lesion was benign glandular epithelium with many goblet cells (Fig. 2, *A*). The proximal line of esophageal resection revealed columnar epithelium which was compatible with the mucosa of the gastric cardia

(Fig. 2, *B*). Additional sections were made to confirm the fact that the normal squamous epithelium had been replaced by this columnar type throughout the length of the resected esophageal segment. No parietal cells were found. An area of perforation was identified just proximal to the tumor.

COMMENTS

This case is of interest for at least two reasons. First, we believe it to be an authentic adenocarcinoma originating in the esophagus, which is not to be confused with the common lesions of this type originating in the gastric cardia and involving the esophagus by direct extension. Second, the presence of normal-appearing glandular epithelium rather than squamous epithelium throughout the specimen, both proximal and distal to the malignant lesion, has interesting embryologic and pathologic implications.

In the human embryo, the trachea separates from the esophagotracheal primordium at about the 4 mm. stage.[9] At this time, both trachea and esophagus are lined by ciliated columnar epithelium, but at about the eleventh week of development, squamous transformation of the esophagus begins, and usually all of the columnar cells have disappeared by the time of birth,[11] although occasionally a full-term infant will exhibit ciliated cells in the esophageal mucosa.[2] In addition to this normal embryologic transition of the esophageal mucosa, we must consider the normal histology of the adult esophagus, which reveals two types of glands. The esophageal glands proper begin to develop during the fourth intrauterine month, and in the adult are found unevenly distributed throughout the length of the esophagus. The glands consist of mucous cells and are located in the submucous layer. The esophageal cardiac glands[11] or Kardiadrüsen,[7] so named because they resemble the glands in the gastric cardia, lie superficial to the muscularis mucosa and are thus differentiated from the normal esophageal glands. These islands of gastric mucosa were first described by Schmidt in 1805.[12] When present, they are found most commonly in the upper portion of the esophagus between the level of the cricoid cartilage and the fifth tracheal ring, but are also frequently seen in a narrow zone just above the esophagogastric junction. Lubarsch[10] considered these areas to be identical to gastric mucous membrane and commented that he had not seen or read of a tumor of or related to these islands of gastric mucosa. Taylor[13] considered these aberrant patches of gastric mucosa in the esophagus to be a type of congenital heterotopia, and he emphasized the fact that all of the different epithelial cells lining the gut arise from the same layer of endoderm, and thus these areas represented a slight error in development. He described six patients who showed patches of gastric epithelium in the esophagus ranging from one-eighth to three-fourths inch in diameter, easily visible at autopsy. His patients varied in age from 7 to 74 years, and he concluded that heterotopic tissue once formed persists indefinitely.

Rector and Connerly[12] reasoned that these islets of gastric mucosa might represent nests of cells destined to form gastric glands. They made microscopic sections of the esophagus in 1,000 consecutive autopsies of infants and children ranging in age from prematurity to 14 years. In sixty-three cases, they ob-

served gastric mucosa without parietal cells, and fifty-six of these areas were located in the upper two-third of the esophagus. Twenty-six patients showed patches of gastric mucosa with parietal cells, and none of these occurred in the distal one-third of the organ. Thus 7.8 per cent of their patients exhibited gastric mucosa in the esophagus, and they believed that a higher figure would have been the result if serial sections had been made. They suggested the role that might be played by these areas in the genesis of carcinoma, papilloma, and peptic ulcer.

CONCLUSION

Review of the literature revealed no case report of such extensive replacement of the normal esophageal mucosa by glandular epithelium as shown in the case reported. The relationship of the adenocarcinoma encountered here to the ectopic epithelium seems too obvious to be coincidental.

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STRESS SYNDROME AND PERFORATED PEPTIC ULCER

Report of Two Cases

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INTRODUCTION

IN HIS classic and prophetic article in 1932, Cushing[1] had marked the hypothalamic area of the brain as significant in the etiology of peptic ulcer. Over a decade later, Dragstedt[2] focused attention on the vagus nerve and the importance of the neural mechanism on gastric secretion. More recently, Seymour Gray and his associates[3] demonstrated the importance of stress and a humoral mechanism through the pituitary-adrenal axis. In 1951, they summarized case reports as well as the results of their own clinical investigation which proved the effect of corticotrophin (ACTH) as well as cortisone on gastric secretion. They were able to show that (1) this medication, in normal subjects, in doses of 100 to 160 mg. daily for a period of three to four weeks, increased the gastric acid secretion to the active duodenal ulcer level, and (2) in patients with peptic ulcer, the administration of 100 mg. of corticotrophin daily produced definite evidence of impending perforation.

It seems to us that the report of Gray heralds a new chapter in the experimental and clinical investigation of peptic ulcer. It may be that the total answer of the pathophysiology of peptic ulcer will come only when we have fully studied and correlated the knowledge of the humoral and neurogenic mechanisms in question. Porter and his associates[4] have made good progress in this direction in their recent work on monkeys. Their results show a true dual influence of the hypothalamus: the first originating in the anterior hypothalamus and being conducted through the vagus and blocked only by vagotomy, and the second originating in the posterior hypothalamus and being conducted humorally through the pituitary-adrenal axis and being blocked only by adrenalectomy. Consequently, we think it important to report two cases in which the stress syndrome caused perforation of a duodenal ulcer: (1) a 42-year-old man who had been on cortisone therapy for three months, and (2) a 6-year-old boy with fractures of the femur and humerus. Neither of these patients gave any previous history of ulcer or indigestion.

Case 1.—A 45-year-old white, male dye tester was admitted on Aug. 18, 1951, with a chief complaint of abdominal pain of nine hours' duration, sudden in onset, generalized, with nausea but no vomiting. For three months prior to admission he had been taking cortisone, 150 mg. daily, for arthritis of the hands and wrists. Blood pressure was 196/106, pulse 112, respirations 24, and temperature 99.4°. He appeared acutely ill, and positive findings were limited to the abdomen, which was distended, tympanitic, and rigid in the

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epigastrium. Liver dullness was present and peristalsis absent. A Levin tube was passed to the stomach for continuous suction. A survey film of the abdomen did not show any free air within the peritoneal cavity. Emergency laboratory studies showed a red blood count of 4,500,000 with 13.2 Gm. of hemoglobin, a white blood count of 11,350 with 76 per cent neutrophils, 23 per cent lymphocytes, and 2 per cent monocytes. A urinalysis was negative. Two hours after admission, celiotomy was performed and a perforated duodenal ulcer closed. The perforation was neatly punched out with little adnexal reaction. In spite of copious gastric content in the peritoneal cavity, the reaction was remarkable in that there was no purulent or fibrinous exudate. Progress during the first eight postoperative hours was poor. A pleural friction rub was heard in the right anterior chest in the fourth intercostal space; he was lethargic, toxic, and hypopyrexic. Circulating eosinophils were 462 per cubic millimeter. In addition to the daily intravenous intake, 20 mg. of ACTH was added to 1 L. of 5 per cent glucose in water, and infused over an eight-hour period.

First Postoperative Day.—Temperature was 99.6° (rectal). He was well oriented, and peristalsis was faintly audible. The circulating eosinophils were 380 per cubic millimeter, plasma chlorides 81 meq. per liter, carbon-dioxide combining power 50 volumes per cent, and blood urea nitrogen 11.4 mg. per cent. Twenty milligrams of ACTH was infused over an eight-hour period in addition to the fluids given for maintenance and correction of the lowered chloride value. During this period the patient became increasingly more alert and comfortable.

Second Postoperative Day.—Temperature was 99.2° (rectal). The patient was resting comfortably with very little pain. The circulating eosinophils were zero. The carbon-dioxide combining power was 48.5 volumes per cent, chlorides 88 meq. per liter, sodium 146 meq. per liter, and potassium 3.4 meq. per liter. An electrocardiogram showed no confirmatory evidence of the potassium deficiency. He was given 500 c.c. of whole blood, 1,000 c.c. of Ringer's lactate, and 500 c.c. of 1.14 per cent potassium chloride for this period.

Third Postoperative Day.—Temperature was 99.6° (rectal). Peristalsis was active; the patient was passing flatus. The Levin tube was removed, and the patient was started on liquid feedings. Laboratory studies were as follows: chlorides 100 meq. per liter and potassium 4.4 meq. per liter.

From this point, the patient's postoperative course progressed satisfactorily, being marred only by a febrile reaction which was due to atelectasis of a portion of the right lower lobe. The patient responded well to expectorants and Terramycin by mouth, and he was discharged on the twenty-first postoperative day on a strict ulcer regimen.

CASE 2.—A 6-year-old white boy was admitted Dec. 22, 1951, because of persistent vomiting of thirty-six hours' duration and epigastric pain. He had been discharged three days previously in a body cast including the left arm and left leg for fractures of the left humerus and femur suffered on Dec. 2, 1951, in an automobile accident. Temperature was 101° (rectal), and he exhibited abdominal rigidity with marked tenderness in the right upper and lower quadrants. Faint peristalsis was audible. A white blood count was 7,700 with 75 per cent neutrophils and 25 per cent lymphocytes, and a red blood count was 4,780,000 with 12.4 Gm. of hemoglobin. Two hours after admission, celiotomy was performed, and a perforated ulcer in the first portion of the duodenum was closed. Postoperatively he was treated with parenteral fluids, blood transfusions, and Wangensteen suction, and he made a good recovery. Hospital convalescence was complicated by pharyngitis and pylorospasm. Further orthopedic procedures delayed discharge until the twenty-fourth day following the abdominal surgery.

COMMENT

We feel that these two cases of perforated duodenal ulcer are probably related to the stress syndrome. In the first case, the prolonged administration of cortisone was a positive factor in this man's ulcer perforation. The fact that

the response to ACTH was so dramatic and efficacious would seem to indicate that the adrenal gland had been made idle by the cortisone medication. Concerning the second patient, we believe that the perforation was due to stress associated with the accident.

SUMMARY

1. The stress syndrome and its relation to peptic ulcer have been discussed.

2. Two cases of perforated peptic ulcer, implicating a humoral etiology, have been presented.

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Editorial

Surgical Anesthesia

THE advances in surgical anesthesia in the last twenty-five years have been phenomenal. The number of anesthetics available, together with the number of supplementary ancillary drugs, gives the anesthetist a wide choice of anesthetics and enables him to carry the patient with a minimum of the anesthetic agent. This is highly desirable and has resulted in a remarkable decrease in our postoperative pulmonary complications.

In spite of this, there are still certain things left to be desired in the management of the surgical anesthetic. Frequently, in an effort to carry the patient "light," the anesthetist allows straining and struggling, which markedly handicaps the work of the surgeon. While it is extremely desirable to give the patient as little of the anesthetic agent as necessary, it is also desirable to have him "deep" enough to enable the surgeon to accomplish the mission which he has set out to accomplish.

A great many anesthetists feel that the patient should be almost awake at the end of the operation. This is fine, provided he does not go into an excitement stage and start struggling on the way back to his room. Patients should have a narcotic as soon as they start moving around during the period of awakening from the anesthesia. It is in this period that they are likely to do their suture line damage. They are still enough under the influence of the anesthetic to be oblivious to pain, and any struggling or jerky movements may break suture lines. If they have the narcotic early, they will sleep the anesthetic off instead of struggling it off. If at the end of the operation they are so light that it is felt they are not likely to stand the trip through long corridors back to their room without struggling, the narcotic should be given before they leave the operating room. If it is not given before they leave the operating room, floor nurses should be instructed to give the narcotic as soon as the patient starts moving or struggling.

It is generally agreed that too much narcosis following operation invites pulmonary complications. After the first dose, narcotics can as a rule be given sparingly. It is the first dose that is important in order to prevent unconscious struggling while the patient is under the influence of the anesthetic agent. By such struggling, abdominal suture lines are often broken and the postoperative hernia starts right then and there. Furthermore, it is probable that a great many inguinal hernias recur before the patient is out of the anesthetic, when injudicious struggling is allowed, thus breaking suture lines. Mattress sutures of heavy black silk in the abdominal fascia have been seen to break with a loud report before the wound was closed, when the patient was

allowed to become light and struggle. One wonders how many times this occurs after the wound has been closed, when the surgeon cannot see what is going on.

At the close of abdominal operations with the patient very light, anesthetists often introduce a catheter to suck out the trachea. This frequently causes spasmodic struggling with its consequent bad effect on the abdominal suture line. At the conclusion of abdominal and hernia operations, the degree of anesthesia of the patient should be discussed by the surgeon and the anesthetist. It should be determined between them whether the best interest of the patient will be served by giving a little more of the anesthetic agent or of some ancillary drug in order to carry the patient back to his room, or whether a narcotic should be administered before he leaves the operating room.

It is obvious that the paramount objective of both the anesthetist and the surgeon is the welfare of the patient. This involves the patient's being kept light enough to maintain physiologic balance but deep enough to prevent interfering with the work of the surgeon.

—*Amos R. Koontz*

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

BLOOD OXYGENATORS: THEORY AND STUDIES IN DESIGN

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GENERAL CONSIDERATIONS OF BLOOD OXYGENATORS

THE current interest in oxygenators stems from the need to divert the circulation from the heart so that intracardiac surgery may be accomplished under direct vision without hurry. This paper discusses the theoretical basis of artificial oxygenators, and presents the results obtained from tests of three particular oxygenators.

Modern Oxygenators.—Most mechanical oxygenators in current use operate by exposing thin films of blood to an atmosphere of oxygen. The *spinning disk oxygenator* of Crafoord described by Björk[1] consists of a series of rotating disks mounted on a common horizontal shaft. As the disks turn, they dip into a pool of blood, forming a film at the periphery of the disk. The film is changed with each revolution. The *spinning screen oxygenator* of Dennis and associates[2] consists of a series of rotating wire mesh disks also mounted on a common horizontal shaft. Blood is distributed onto each disk near its center, and is filmed over the whole surface of the disk by gravity and centrifugal action. In the *stationary screen oxygenator* of Miller and co-workers,[3] blood flows by gravity down a set of stationary, vertically oriented wire mesh screens. The *Stedman packing oxygenator* of Bailey[4] consists of a stack of horizontal perforated and embossed wire mesh plates. The blood flows downward through the stack while oxygen is passed upward. In the *Archimedes' spiral oxygenator* of Joengbloed,[5] the blood is filmed on the inside surface of a tube which is wound into a helix. The blood film is propelled forward through the tube when the helix is rotated about its axis.

These oxygenators disperse blood in oxygen. Other oxygenators, however, disperse oxygen in the blood. In the *small bubble oxygenator* of Clark and associates,[6] minute oxygen bubbles are introduced into the blood. The blood and residual bubbles are then passed through a chamber filled with Antifoam†-coated polyethylene shreds. Here the small bubbles coalesce, and a separation

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of the blood from the residual gas is effected. Lary[7] uses even smaller bubbles, but manages to dispense with defoaming facilities by avoiding an oxygen surplus. This apparatus is the purest of "oxygenators," since no carbon dioxide can be eliminated. Thomas'[8] *large bubble oxygenator* uses bubbles large enough to separate from the blood by buoyancy. In the *foam oxygenators* of Waud[9] and Gimbel and Engelberg,[10] the blood is oxygenated as it cascades down a densely packed column of foam.

Physical and Chemical Aspects of Gas Exchange.—Oxygen is carried by the blood both as a solute and as oxyhemoglobin within the erythrocytes. The quantity of oxygen which is dissolved in the plasma is normally about one-fiftieth of that bound by the hemoglobin, and will at normal barometric pressures be neglected in considering the oxygen-carrying capacity of blood.

The combination of hemoglobin and oxygen may be represented by the equation

$$Hb + O_2 \rightleftharpoons HbO_2 + \text{Heat.}$$

From this equation it is apparent that a high oxygen tension and a low temperature favor the formation of HbO_2. This equilibrium is also influenced by the pH (Bohr effect). As the pH drops, the reaction moves toward the left. At an oxygen tension of 100 mm. Hg and normal pH, hemoglobin is approximately 97 per cent saturated.

The erythrocyte equilibrates with great rapidity with the oxygen tension of the adjacent plasma.[11] In the subsequent discussion it will therefore be assumed that the oxygen tension in the erythrocyte and in the plasma is the same.

The fundamental problem involved in the operation of blood oxygenators is the transfer of oxygen across a gas-blood interface. If blood and oxygen were exposed to one another without any turbulence within the liquid or gas, movement of the gas would depend solely on the kinetics of the individual gas molecules. This process is generally referred to as molecular diffusion. When the gas and liquid phases are subject to turbulence, the process is called eddy diffusion. Eddy diffusion, more rapid because distribution occurs through mixing, is the transfer mechanism of mechanical oxygenation. The situation is that of a gas phase and a liquid phase in contact at an interface, each of which has associated with it a certain degree of turbulence. The partial pressure of the oxygen in the gas phase is P_G and that in the liquid phase is P_L. If N_{O_2} equals the number of oxygen molecules which enter the plasma per unit time, then

$$N_{O_2} = K_{O_2} A \ (P_G - P_L)$$

where A is the area at the interface.

The factor K increases with turbulence and temperature.

Several observations may be made about the preceding equation:

1. *Turbulence:* In order to explain the variation of K with turbulence, two films—one consisting of stagnant gas, the other of stagnant liquid—are postulated at the interface.[12] The gas traverses these films by the relatively slow process of molecular diffusion, which is the rate-limiting factor

in the oxygenation process. The greater the turbulence in each phase, the thinner these films become, with a consequent increase in the diffusion rate across the interface. Certain phases offer more resistance to eddy diffusion than others. It is of particular importance to provide turbulence to the high resistance phase. In blood oxygenators, the resistance of the blood phase is large compared to that of the gas phase, a phenomenon which is said to be due to the low solubility of oxygen in plasma.[12] Producing turbulence in the blood results in a substantial increase in the speed of oxygenation, while turbulence in the gas phase has practically no effect.* In the *vertical cylinder oxygenator,* a several-fold increase in oxygenation is noted when wire mesh screens are used instead of smooth metal plates.[13] This may be attributed to the turbulence produced by the blood flowing down the uneven wire mesh surfaces.

2. *Temperature:* With increasing temperature, the factor K in the diffusion equation becomes larger, and this increases the rate of diffusion. On the other hand, at higher temperatures, oxyhemoglobin is more dissociated. This results in a greater value of P_L for any given saturation, with a consequent decrease in the rate of diffusion. In all perfusion systems, P_G is maintained at a value quite far above the value of P_L which is required for complete saturation. Under these conditions, the increase in K considerably outweighs the decrease in $P_G - P_L$, and the net result is an increase in the rate of oxygenation with increasing temperature.[1] However, since the oxygen requirements of the perfused subject also vary with his temperature, it is questionable whether the subject's oxygen debt is reduced by oxygenating the blood at, say, 37° C. instead of 30° C.

3. *Oxygen tensions:* The equation shows that the rate of diffusion is proportional to the difference in oxygen tensions between the gas and liquid phases. The value of P_G is directly proportional to the absolute pressure of the ventilating gas. Thus, operating the oxygenator above atmospheric pressure increases the rate of diffusion. If the blood becomes saturated with oxygen under these conditions, some of the dissolved gas may be expected to come out of solution when the blood is returned toward atmospheric pressure. Whether a limited amount of minute oxygen bubbles would be injurious is uncertain. On the other hand, operating the oxygenator below atmospheric pressure allows simplification of the extracorporeal circuit. Because in this case the oxygenator may draw its own blood, the pumps that carry the blood from the veins and from the coronary sinus of the opened heart may be dispensed with. The decrease in rate of oxygen diffusion is compensated by the reduced blood holdup resulting from the elimination of two pumps.

Carbon Dioxide Elimination.—It is desirable, although it does not appear to be essential in short-term perfusions, to maintain a constant pH in the blood by eliminating CO_2 at an appropriate rate. The equation which describes CO_2

*Since the pulmonary capillaries are approximately the same diameter as the erythrocytes, it is not unreasonable to suppose that the layer of stagnant plasma adjacent to the capillary wall is swept away as the erythrocyte squeezes through. From the previous considerations, this should make a material contribution to the gas exchange.

elimination is

$$N_{CO_2} = K_{CO_2} A \ (P'_L - P'_G)$$

where P′ represents the partial pressure of CO_2, and K_{CO_2} is the proportionality constant. From data for the diffusion of O_2 and CO_2 through water, K_{CO_2} is estimated to be approximately twenty-five times K_{O_2}. This explains why elimination of CO_2 may be readily achieved in spite of the fact that the diffusion gradient can never exceed the plasma CO_2 tension (normally 40 mm. Hg). In film oxygenators, CO_2 elimination usually surpasses formation unless P'_G is maintained between 1 per cent and 3 per cent in the ventilating gas. In the bubble and foam oxygenators, however, the gas flow may be limited by the capacity of the defoaming system, so that adequate CO_2 elimination may not be achieved. However, the debt in CO_2 elimination tends to be self-limiting because as the CO_2 tension mounts, the available gas can transport a larger quantity.

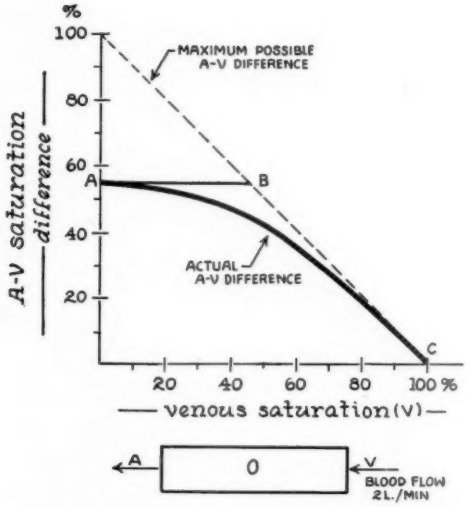

Fig. 1.—Saturation gain of a typical oxygenator as a function of the saturation of the venous blood.

Work Function.—Consider a typical oxygenator *O* (Fig. 1), through which blood is flowing at a constant rate. The performance of this oxygenator at varying venous saturations is shown by the heavy line, the *A-V difference* in per cent of saturation being plotted against the *venous saturation (V)* in per cent. The dotted line, representing 100 – V, indicates the maximum increase in saturation possible for any V. If the oxygenator were equally effective at all saturations, it might be anticipated that the path of performance for bloods of varying venous saturations would follow the line *ABC*. Thus, equal increments of oxygen would be added up to the point *B*, after which the arterial blood would always be saturated. The actual path of the oxygenator, however, described by the heavy line, is seen to lie below the anticipated performance. What is the explanation for this defection?

There are two reasons for dropping off oxygenation at higher saturations:

1. Since at higher saturations the average value of P_L in the diffusion equation is greater, there will be a decrease in the rate of diffusion. However, changes in P_L have little effect on the rate of oxygenation when P_G is of the order of 700 mm. Hg. With pure oxygen at atmospheric pressure, the loss in diffusion gradient as blood passes from 0 to 80 per cent saturation is 5 per cent. Hence, this does not explain the relatively large decline in oxygenation which is actually encountered.

2. The important factor arises because, unlike pulmonary capillaries, the films of present-day oxygenators are several erythrocytes thick. Only the plasma and erythrocytes actually at the gas-blood interface are immediately exposed to the oxygen; the deeper blood is relatively anoxic. Blood is at the interface for a certain time, T, characteristic of the particular apparatus, before turbulence remixes it with the subsurface blood. When T is longer than is required to saturate the film, exposure time will be wasted.

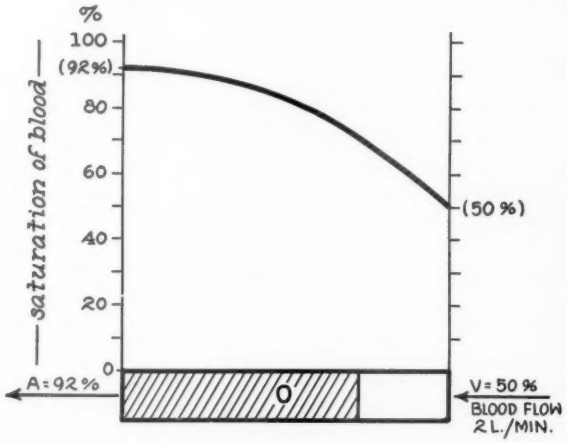

Fig. 2.—Saturation of blood as a function of distance through the oxygenator. In the region of the oxygenator indicated by shading, each film is exposed for a longer time than is necessary for it to absorb all the oxygen it can carry.

In Fig. 2 we show an oxygenator which at a flow of 2 L. per minute takes blood from a venous saturation of 50 per cent to an arterial saturation of 92 per cent. As the blood moves along the oxygenator, the saturation of the blood increases from 50 to 92 per cent. Hence, under steady-state conditions it should be possible to associate with every point along the oxygenator a particular saturation between 50 and 92 per cent. In Fig. 2 the saturation has been plotted as a function of the distance along the oxygenator. Consider the point in the oxygenator at which the saturation is 60 per cent. The film exposed at this point cannot increase more than 40 per cent in saturation. If the time T is such that the saturation of the film can increase only 30 per cent, then up to the point along the oxygenator where the average saturation becomes 70 per cent, each film will introduce an equal quantity of oxygen corresponding to a saturation difference of 30 per cent. Above 70 per cent, each film is exposed longer than is necessary for it to pick up the maximum amount of oxygen it can carry, and hence the oxygenation process becomes less effi-

cient. Thus, the rate of oxygenation decreases at higher saturations because the film exposure time is progressively wasted as the capacity of the film to take oxygen falls. Karlson and associates[14] encountered the same phenomenon when they observed that, when oxygenating blood by filming it on the inside of a vertical revolving cylinder, the saturation at any given blood flow did not increase in proportion to the height of the cylinder. In one experiment, blood flowing at 200 ml. per minute into a certain cylinder rose in saturation from 68 to 86 per cent, an increment of 18 per cent. When the cylinder was doubled in length, the additional increment in saturation was only 7 per cent.

It becomes desirable to find a criterion by means of which it is possible to determine the relative difficulty or "work" involved for a given oxygenator in going from one level of saturation to another. Specifically, we are interested in a function W, which we may call the "work function," which will associate with every level of saturation a number in such a way that the relative difficulty for oxygenating blood from a saturation S_V to a saturation S_A, is proportional to the difference $W_A - W_V$ of the work functions for the two saturations.

Table I lists the work function for the spinning disk oxygenator. This was obtained as will be described in the section on this apparatus. As an example of the use of the work function let us consider the relative difficulty of oxygenating from 40 per cent to 70 per cent as compared to 65 per cent to 95 per cent. As shown in Table I, the difference in work function between 40 per cent to 70 per cent is 70.6 – 40.9, or 29.7, work function units (wfu). Similarly for the interval 65 to 95 per cent, the work done is 115.9 – 65.4 = 50.5 wfu. The relative difficulty of oxygenation in the two regions is $\frac{50.5}{29.7} = 1.7$.

TABLE I. WORK FUNCTION FOR SPINNING DISK AND STEDMAN PACKING OXYGENATOR (BEEF BLOOD AT 37° C., 95 PER CENT O_2, 5 PER CENT CO_2 AT 760 MM. HG)

SATURATION PER CENT	WORK FUNCTION (wfu)	SATURATION PER CENT	WORK FUNCTION (wfu)
15	22.4	76	77.3
20	25.6	78	79.8
25	29.0	80	82.3
30	32.8	81	84.0
35	36.7	82	85.2
40	40.9	83	86.8
42	42.6	84	88.0
44	44.3	85	90.0
46	46.1	86	91.7
48	48.0	87	93.4
50	50.0	88	95.5
52	52.1	89	97.4
54	54.3	90	100.0
56	56.3	91	102.1
58	58.2	92	105.7
60	60.3	93	108.6
62	62.3	94	111.7
64	64.3	95	115.9
66	66.4	97	124.5
68	68.3	99	135.9
70	70.6		
72	72.7		
74	74.8		

Suppose now that an experiment shows that the spinning disk oxygenator at a certain blood flow rate oxygenated the blood from 40 per cent to 70 per cent. The question might arise: What would have been the arterial saturation had the venous saturation been 65 per cent? We have seen that the work done in the 40 per cent to 70 per cent interval is 29.7 wfu. Hence, we are dealing with an oxygenator which is capable of an output of 29.7 wfu. The work function of 65 per cent is 65.4 wfu. To this we add the work done, 65.4 + 29.7 = 95.1 wfu, and thus obtain the work function of the arterial blood for this case. Table I shows the saturation corresponding to 95.1 wfu to be 88 per cent. This then would be the arterial saturation with an input of 65 per cent venous blood.

The familiar form for expressing the oxygenation accomplished by an apparatus is the volume of oxygen introduced per minute. The appropriate formula is:

$$\text{Flow (in 100 ml./min.)} \times \frac{(\text{final saturation in \%} - \text{initial saturation in \%})}{100} \times \text{oxygen capacity of the blood (in ml. } O_2\text{/100 ml. of blood)} = O_2 \text{ introduced (in ml./min.).}$$

It is apparent from this formula that there is an inverse relationship between the saturation increase and the oxygen capacity (hemoglobin concentration) of the blood; other conditions remaining the same, the more anemic the blood, the greater will be the saturation change. Since oxygenation is easier at lower saturations, as has been already discussed, oxygen introduced cannot provide a unique description of the oxygenating capacity at different saturation ranges. Work function units are, in effect, saturation units corrected to give a unique description of the oxygenator in question which is independent of the saturation range. Therefore, if the final and initial work functions are substituted for the final and initial saturations in the preceding formula, the resulting equation becomes independent of the saturation range:

Flow (in 100 ml./min.) × (final work function – initial work function) × oxygen-capacity of the blood (in ml. O_2/100 ml. blood) = work function introduced (in work function units).

Application of this formula makes possible the comparison of experiments performed with bloods of different hemoglobin concentrations or in different saturation ranges.

Example: An oxygenator will raise the saturation of blood of 20 volumes per 100 ml. oxygen capacity flowing at 3.0 L. per minute from 40 per cent to 70 per cent saturation. What final saturation might be anticipated for blood of 16 volumes per 100 ml. oxygen capacity flowing at the same rate and starting at a saturation of 60 per cent?

Steps: 1. Calculation is made of increase in work function units. The work function of the initial saturation is subtracted from that of the final saturation.

2. Work function units introduced are obtained by multiplying flow × increase in work function units × capacity.

3. Solve for unknown new wfu increase; add to wfu of new initial saturation; then convert sum to corresponding saturation.

a. 70 per cent saturation – work function	70.6 wfu
40 per cent saturation – work function	40.9 wfu
	29.7 increase

in work function units.

b. $30 \times 29.7 \times 20 = 11{,}880$.

c. $30 \times X \times 16 = 11{,}880$.

d. $X = 37.1$ work function units.

Work function of 60 per cent = 60.3 wfu.

60.3 + 37.1 = 97.4 wfu.

Saturation analogue of 97.4 wfu is 89 per cent saturation. It is important to note that such calculations are based on assumptions that are only approximately true. It is assumed that the work function of the oxygenator is exactly known, and that the work function and the efficiency do not change within the range of hemoglobin concentrations encountered. Since these assumptions are not entirely correct, the calculations based on them can only be approximations. The question arises as to the applicability and usefulness of the work function described. Does it apply to different oxygen tensions and to different oxygenators? Since the function is obtained empirically, only experiments can define its applicability. Thus, it appears that the function used previously also describes the performance of the Stedman packing oxygenator. However, a different function is obtained with the foam oxygenator. Large variations in the gas oxygen tension also change the function. Experiments have shown the variations in performance at various blood flows to be too large to permit the comparison of experiments in which flow changes.

Practical Considerations of Mechanical Oxygenators.—The ideal oxygenator accomplishes its work while holding a relatively small amount of blood. It should be simple, safe, and reliable.

Holdup: The blood holdup of an oxygenator may be defined as the entire blood volume which is within the oxygenator during its operation. This includes blood volume which is in the oxygenator distributor, in the collecting pool, and in the defoaming chamber if present. In most oxygenators the holdup varies with the blood flow rate. In the case of the film oxygenators, this results from a thickening of the film, in the foam oxygenator, from a wider separation of the bubbles. It is inevitable that as the oxygenator gains blood, the subject loses it, and vice versa.

Miller and co-workers[3] have been able to overcome fluctuations in blood volume due to holdup by use of a recirculating pump which maintains a constant flow of blood through the oxygenator.

Comparative efficiency: Karlson and associates[14] introduced the concept of comparative efficiency as a criterion for the comparison of different oxygenators. The efficiency was defined as the ratio of the milliliters of oxygen introduced into 100 ml. of blood per milliliter of blood film holdup. To make this definition unique, several additional specifications should be made. First, since the efficiency of most oxygenators varies with the blood flow rate, this should be stated. Second, the holdup used in the definition should be the total

holdup in the oxygenator, including the systems which distribute the venous blood and collect the arterial blood. Third, since the amount of oxygen introduced is influenced by the degree of venous saturation (the work function consideration), the venous saturation should be specified. In view of these considerations Karlson's definition might be modified to read: *The comparative efficiency of a blood oxygenator is the ratio: the largest flow of blood of 15 Gm. per cent hemoglobin which can be raised from 60 to 90 per cent saturation*/the total holdup at that flow rate.*

The comparative efficiencies of the oxygenators described in this paper are presented for purposes of comparison in the summary. These efficiencies are an index of the amount of oxygen which an oxygenator is capable of introducing into blood for a given amount of holdup. Since any oxygenator can be made to produce an arbitrary saturation change for an arbitrary blood flow, provided it is made large enough, it is clear that efficiency is simply an index of the relative holdup. To lay stress on a small holdup may appear unreasonable when one considers the use of these oxygenators for operations where cost and availability of donor blood do not play an important part. There are, however, a number of other considerations which give the question of holdup its importance. First, the more donor blood that has to be used, the graver the danger of transfusion reactions and serum hepatitis. Second, the greater the holdup, the greater the problem of homeostasis; a small fluctuation in holdup becomes a significant variation in the subject's blood volume. Third, in experimental surgery the obtaining of large quantities of donor blood becomes a time-consuming annoyance.

Film characteristics: In the stationary screen oxygenator and the Stedman packing oxygenator, the blood tends to course down in channels without wetting the surface evenly and making full use of the filming surface. Such oxygenators show an improved performance if the filming surfaces are completely flooded with saline solution prior to the admission of blood, and if the surfaces are kept wet with blood throughout the perfusion by means of a recirculating pump.

In the spinning disk oxygenator, on the other hand, good filming is obtained without special measures.

Blood trauma: Hemolysis, as an index of trauma to the blood, is not a problem with the oxygenators under discussion. All oxygenators decrease the platelet count of the circulating blood to some extent, but little comparative information is available.

Humidification and heating of the gas: Many heart-lung machines provide for the heating and the humidification of the oxygen prior to its entrance into the oxygenator. To decide whether it is desirable to incorporate accessories for this purpose, the following facts should be taken into consideration:

The saturation of 1 L. per minute of dry gas results in a loss of about 3 Gm. of water per hour from the blood. The heat of vaporization of 3 Gm.

*This saturation range, arbitrarily chosen, combines the virtues of clinical interest and experimental sensitivity.

of water represents a loss of 1.6 kilogram calories. If this gas must also be warmed from room temperature to 37° C., an additional 0.3 kilogram calorie per hour will be lost from the blood.

Warming and humidifying 1 L. of dry cool gas per minute therefore represents a loss of 1.9 kilogram calories per hour, or approximately 6 per cent of the heat production of a 20 kilogram subject.

EXPERIMENTAL STUDIES IN OXYGENATOR DESIGN

Experimental Techniques (General).—To achieve precision in the technique of evaluating oxygenators, in vitro tests with beef blood were carried out. This made it feasible to hold a steady state and to control the flow and saturation of blood entering the apparatus, and was of great value in obtaining data under controlled conditions.

Fifteen to thirty liters of beef blood were collected in one-fifth their volume of citrate-dextrose solution at an abattoir. The hemoglobin concentration of the citrated blood was between 9 and 12 Gm. per cent. In order to make the results immediately applicable to normal blood, the data presented were corrected by means of the work function to a hemoglobin concentration of 15 Gm. per cent. Penicillin was added to the blood. Experiments and analyses were completed within eight hours of the bleeding. The experiments were carried out in a constant temperature hood at 37° C.

To provide unsaturated blood for testing, the Stedman packing column, to be described subsequently, was employed. The blood was recirculated through the column, which was ventilated by either 5 per cent CO_2-95 per cent N_2, or by 100 per cent CO_2 followed by 100 per cent N_2. The 5 per cent CO_2-95 per cent N_2 mixture was preferred since the CO_2 tension was thereby maintained at 36 mm. Hg tension and variations in Bohr effect were avoided. Pure carbon dioxide followed by pure nitrogen to return the pH to the normal range proved the more rapid method, however. No precise method was available for producing any desired unsaturation for study; approximations could be achieved on the basis of experience.

Sufficient unsaturated blood was prepared so that conditions within the oxygenator would be in a steady state for at least three minutes before samples were taken. The oxygenator was ventilated with 95 per cent O_2-5 per cent CO_2 at a flow of 7 L. per minute, unless otherwise noted. Constant, reproducible blood flows were obtained by driving the blood by direct air pressure, adjusted by a solenoid, mercury pressure switch combination, to maintain a uniform pressure drop across a resistance in the blood circuit leading to the oxygenator. Samples of the blood before and after passage through the oxygenator were analyzed in duplicate. When carbon dioxide and oxygen determinations were desired, the technique of Van Slyke was employed. In general, however, analyses were for oxygen only; these were performed spectrophotometrically by the technique of Gordy and Drabkin,[15] modified to hemolyze the blood as suggested by Hickman and Frayser.[16] Hemolysis was obtained under anaerobic conditions by using a three-way stopcock for adding the saponin solution and mercury. The hemolyzed samples were examined in cuvettes having a 1 mm. light path in a Beckman DU spectrophotometer.

An attempt was made in each experiment to adjust the conditions of blood flow and oxygenator so that an increase in saturation of at least 20 per cent would be achieved. This minimized the influence of experimental or analytic inaccuracies. In view of work function considerations, testing is less sensitive when blood leaves the apparatus at saturations over 90 per cent, and this range was generally avoided.

Experimental Techniques Used for the Spinning Disk Oxygenator.—
Ranges studied:

Holdup:	500 to 900 ml.
Disk speed:	50 to 125 r.p.m.
Oxygen tension:	700 and 1,000 mm. Hg.

Because of the nature of this oxygenator, a simple and informative testing procedure is available that cannot be readily applied to other oxygenators. It is true of all circulatory systems that, provided the fluid moves along with even progression and without channeling or dallying in stagnant pools, the following formula applies:

$$\frac{\text{Volume of a chamber in the circuit}}{\text{Transit time of fluid through the chamber}} = \text{flow of fluid through circuit.}$$

Thus, any particular minute flow will designate what the transit time through a chamber of given volume must be; a blood flow of 2,000 ml. per minute through an oxygenator of 500 ml. content will require a transit time through the oxygenator of fifteen seconds. Hence, the oxygenation of 500 ml. of stationary blood achieved in fifteen seconds should be equivalent to that obtained with an active circulation of 2,000 ml. per minute.

A collecting catheter of low dead space is placed at the bottom of the oxygenator in a central location. The desired volume of blood is placed in the oxygenator and reduced to a low saturation by passing 5 per cent O_2 – 95 per cent N_2 above the rotating disks. The disks are stopped, the atmosphere is flushed with 5 per cent CO_2 – 95 per cent O_2, and the disks are rotated once more. Five milliliter blood samples are collected at the rate of 1 ml. per second, with five seconds intervening between samples, so that there are six samples per minute and each mirrors the average saturation of a five-second interval. The experiments are made with varying amounts of blood in the apparatus and varying rates of disk rotation. When the saturations are plotted against time, the change in saturation for any exposure time may be read, and the change in saturation at the flow rate corresponding to the exposure time estimated.

Experimental Techniques Used for the Stedman Packing Oxygenator.—
Ranges studied:

Column height:	0.25 to 2.75 feet.
Blood flow:	200 to 5,200 ml. per minute.
Oxygen tension:	700 and 1,000 mm. Hg.

Holdup in the Stedman packing oxygenator was determined by passing blood at varying flow rates through two feet of packing that had been removed from its casing. When a steady state was achieved, the isolated packing was weighed; the holdup was obtained by subtracting the weight of the dry packing.

Experimental Techniques Used for the Foam Oxygenator.—
Ranges studied:

Column height:	1 to 3 feet.
Blood flow:	600 to 3,000 ml. per minute in 1½ inch diameter column.
Oxygen tension:	140 and 700 mm. Hg.
Gas flow:	100 to 3,500 ml. per minute in 1½ inch diameter column.
Column diameter:	1.5, 2, 3 inches.
Bubble orifices:	Sizes 17, 20, 21, 23, 25 hypodermic needles.

The work function for the foam oxygenator was determined as follows: The blood was passed at a rate of 1,000 ml. per minute into a 12 inch high, 1½ inch diameter column using 25 gauge hypodermic needles for gas dispersion. The gas used was a mixture of 95 per cent O_2-5 per cent CO_2. Batches of blood having venous saturations varying between 24 and 64 per cent were passed through the oxygenator. Holdup in the foam oxygenator was determined at varying gas and blood flows in a 1½ inch diameter, three-foot-high column by simultaneously closing the inlet and outlet of the oxygenator and then measuring the volume of the defoamed blood.

THE SPINNING DISK OXYGENATOR

Description of Apparatus.—The oxygenator tested was closely modeled on that employed by its originator, Crafoord.[1] The oxygenator (Fig. 3) consists of a horizontal cylinder with blood entering at one end and leaving at the other. Within the cylinder are a series of fifty disks of 19.7 cm. diameter, mounted 0.4 cm. apart on a horizontal shaft. The disks dip into the blood that is in transit through the cylinder so that an annular film of blood forms at the periphery of the disk. Oxygen is passed through the space above the blood. There are two principal variables in the use of the apparatus: 1. The height or amount of blood in the oxygenator determines the width of the annular film on the disk and also the segment of the disk which will be exposed to the oxygen above the surface of the blood. 2. The rate at which the disks rotate determines the frequency with which the films are renewed in the blood trough.

Practical Operation.—The more blood that is present in the oxygenator and the more rapidly the disks rotate, the greater is the tendency toward formation of foam and the formation of films that bridge from one disk edge to the next. The apparatus cannot be rotated at a peripheral speed of 130 cm. per second (125 r.p.m.) for more than short periods of time without prohibitive foaming, and 110 cm. per second (105 r.p.m.) was found to be the highest speed for practical operation, although even here a few bubbles formed. Smearing Dow-Corning Antifoam on the inside of the cylinder and along the disks did not prove helpful.

An increase in blood content of the oxygenator from 800 to 900 ml. causes a rise of 4 mm. in the level of blood in the cylinder. The task of keeping constant the blood volume of the oxygenator, and therefore of the subject, becomes difficult, since most control devices employ changes in blood height as their reference.

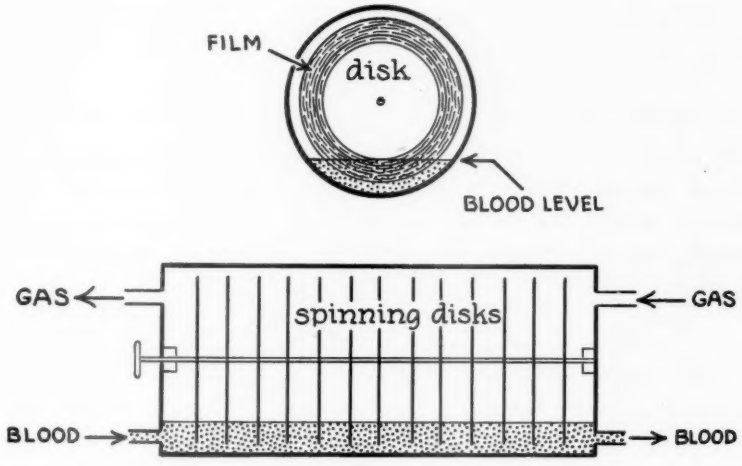

Fig. 3.—Spinning disk oxygenator: schema.

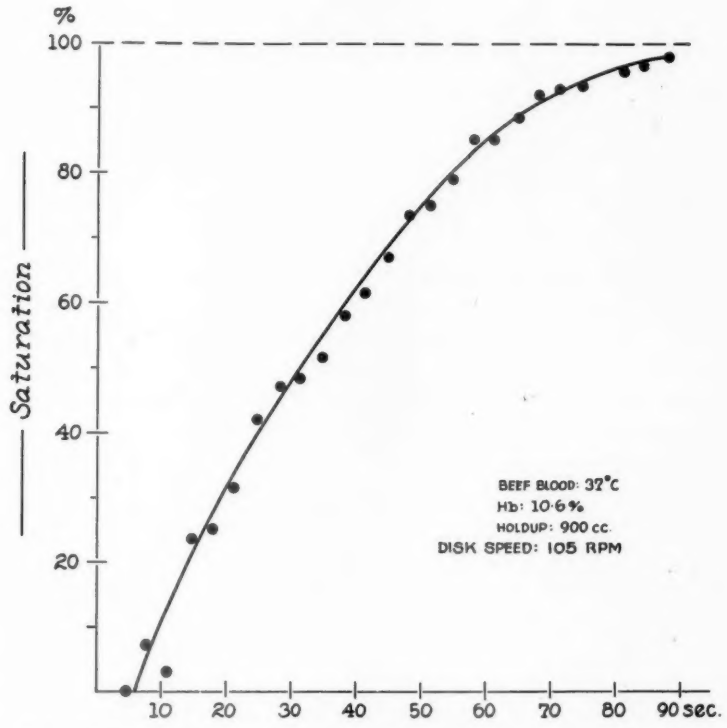

Fig. 4.—Spinning disk oxygenator: saturation as a function of film exposure time.

Results.—The characteristics of the spinning disk oxygenator have been described in detail in a comprehensive monograph by Björk.[1]

Work function: Fig. 4 plots saturation versus time for 900 c.c. of beef blood at 37° C. in the spinning disk oxygenator operating at 105 r.p.m.

Take two saturations, S_1 and S_2, on this curve and let the corresponding times be T_1 and T_2. Since the time interval, $T_1 - T_2$, is indicative of the relative difficulty in oxygenating from S_1 to S_2, we define the difference in work function $W_1 - W_2$ between the two levels of saturation as

$$W_1 - W_2 = C\ (T_1 - T_2)$$

where C is an arbitrary constant. However, to provide a basis of comparison for various work function curves of different oxygenators, the work function level of 50 per cent saturation has been arbitrarily set at 50 work function units (wfu), the 90 per cent saturation level at 100 wfu. This determines the value of C. The work function for the spinning disk oxygenator is given in Table I.

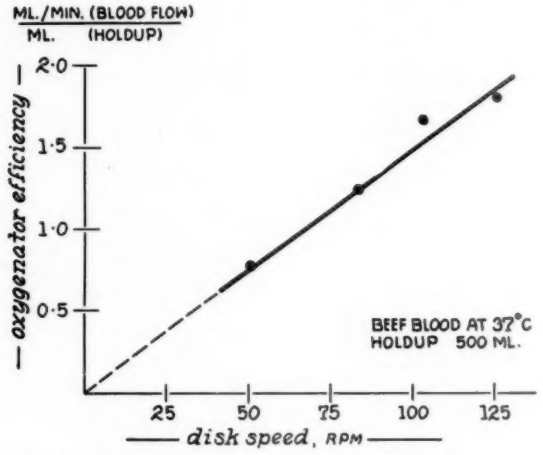

Fig. 5.—Spinning disk oxygenator: efficiency as a function of disk speed.

Overpressure operation: Two experiments were performed in which the oxygen tension was 1,000 mm. Hg instead of 700 mm. Hg (Table II). These experiments may be compared with those in which 900 ml. of beef blood at 37° C. was exposed at a disk rotation rate of 105 r.p.m., since the conditions were identical except for the oxygen pressure. The time required for hemoglobin saturation to rise from 50 to 90 per cent is almost exactly inversely

TABLE II. SPINNING DISK OXYGENATOR; OXYGENATION AS A FUNCTION OF OXYGEN TENSION (BEEF BLOOD, 900 ML., 105 R.P.M., 37° C.)

EQUIVALENT FLOW (50–90%) (ML./MIN.)	GRADIENT O_2 (MM. Hg)
2,850	940
2,000	630
Ratio: 1.42	1.50

proportional to the oxygen gradient. Consequently, the corresponding blood flow is directly proportional to the gradient. This correlation of oxygenation power with oxygen tension of the gas is predicted by the diffusion equation and demonstrated experimentally by Björk[1] for oxygen tensions below 700 mm. Hg.

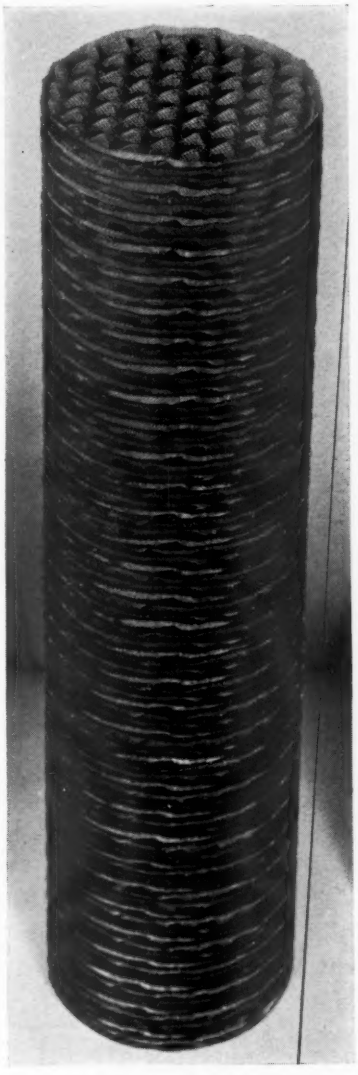

Fig. 6.—Stedman packing oxygenator.

Efficiency: The comparative efficiency of our spinning disk oxygenator with a holdup of 900 ml. and at 105 r.p.m. was $\frac{1.7 \text{ ml./min. (blood flow)}}{\text{ml.} \quad \text{(holdup)}}$. The comparative efficiency of Björk's oxygenator is estimated at $\frac{1.0 \text{ ml./min.}}{\text{ml.}}$. The difference between these two oxygenators may be attributed to the fact that our disks were 19.7 cm. in diameter, while Björk's disks were 13 cm. in diameter.

Thus our minute area per disk was 2.6 square meters per minute, while Björk's minute area per disk was about 1.5 square meters per minute.

The linear variation of efficiency with disk speed (Fig. 5) concurs with the findings of Björk.[1] Thus the efficiency of this oxygenator is limited by the highest disk speed at which it can be operated without foaming.

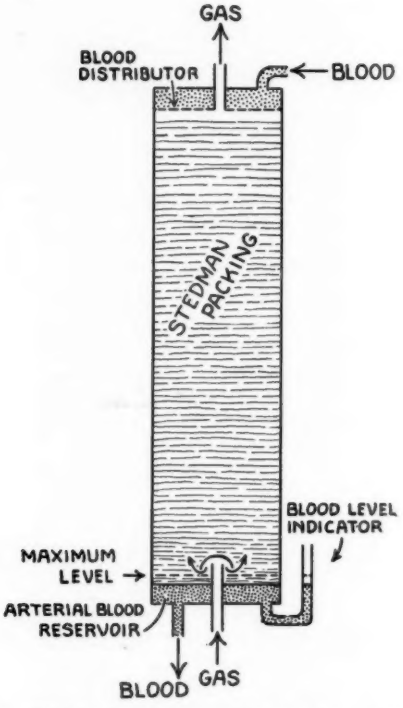

Fig. 7.—Stedman packing oxygenator: schema.

THE STEDMAN PACKING OXYGENATOR

Description of Apparatus.—The Stedman packing oxygenator was introduced by Bailey.[4] Stedman packing is a tower packing used by the chemical industry in processes requiring intimate contact between liquids and gases. It consists of stacks of 60 by 40 mesh stainless steel wire cloth disks of six-inch diameter. Each wire disk is embossed and perforated so that it presents a pattern of pyramids, valleys, and holes (Fig. 6). There are 100 disks per foot of column height, providing an effective area of thirty-four square feet. Blood is distributed at the top of the column, and flows downward in a continuous stream from disk to disk. The oxygen is delivered at the bottom of the column, just above the blood pool that runs off the column. A tight fit between the disks and the casing assures that the oxygen passes upward through the disks. A diagram of this oxygenator is shown in Fig. 7.

Practical Operation.—The oxygenator does not foam since there are no moving parts and the oxygen moves past the blood rather than through it. If the sheets are not wet, the filming of the blood is imperfect because of channeling. Since the sheets are spot-welded together, it is possible to inspect

only the exterior surfaces, and it is necessary to rely on strong alkaline solutions for cleanliness.

TABLE III. WORK ACCOMPLISHED AS A FUNCTION OF COLUMN HEIGHT FOR THE STEDMAN PACKING

RUN NO.	BLOOD FLOW (ML./MIN.)	DIFFERENCE IN WORK FUNCTION (wfu)	RATIO OF DIFFERENCE IN WORK FUNCTION	COLUMN HEIGHT (FT.)	RATIO OF COLUMN HEIGHT
G3	4,000	52.1	1.84	2.75	1.84
H6	4,000	28.4		1.50	
H2	2,700	32.5	1.52	1.50	1.50
D5	2,700	21.4		1.00	
H1	1,330	51.3	1.42	1.50	1.50
B5	1,400	36.2		1.00	

Results.—

Work function: The work function for this oxygenator is given in Table I. The identity of the work functions of the spinning disk and Stedman packing oxygenators was established by the close correlation prevailing between the experimental results obtained for the Stedman packing oxygenator and those predicted by the work function of the spinning disk oxygenator.

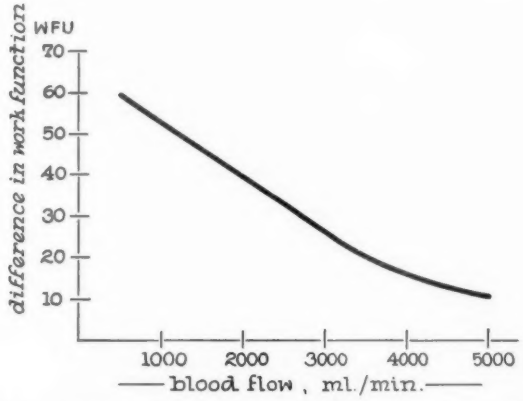

Fig. 8.—Stedman packing oxygenator: work done as a function of blood flow.

For example, since each disk in the column may be considered an individual oxygenator, the difference in work function produced by a column may be expected to be proportional to the column height. In Table III, pairs of experiments performed at the same flow but at different column heights are listed. The ratio of the column heights and the ratio of the change in work function are substantially equal.

Oxygenating characteristics: The change in work function which this oxygenator accomplishes per foot of column height is shown as a function of blood flow in Fig. 8. This curve can be used to estimate the change in saturation of blood at various flow rates. To illustrate its use, suppose one wishes to estimate the approximate length of column required to oxygenate a 2 L. per minute flow of blood from a saturation of 70 per cent to 95 per cent. Table I

shows the required change of work function to be 115.9 – 70.6 = 45.3 wfu. From Fig. 8 it is seen that the work done by one foot of six-inch diameter packing at a flow of 2 L. per minute is 40 wfu. The length of column needed then is 45.3/40.0 = 1.1 feet.

Holdup: The holdup of blood in the packing at varying flow rates is shown in Fig. 9. This curve is linear within the range of anticipated flows. When

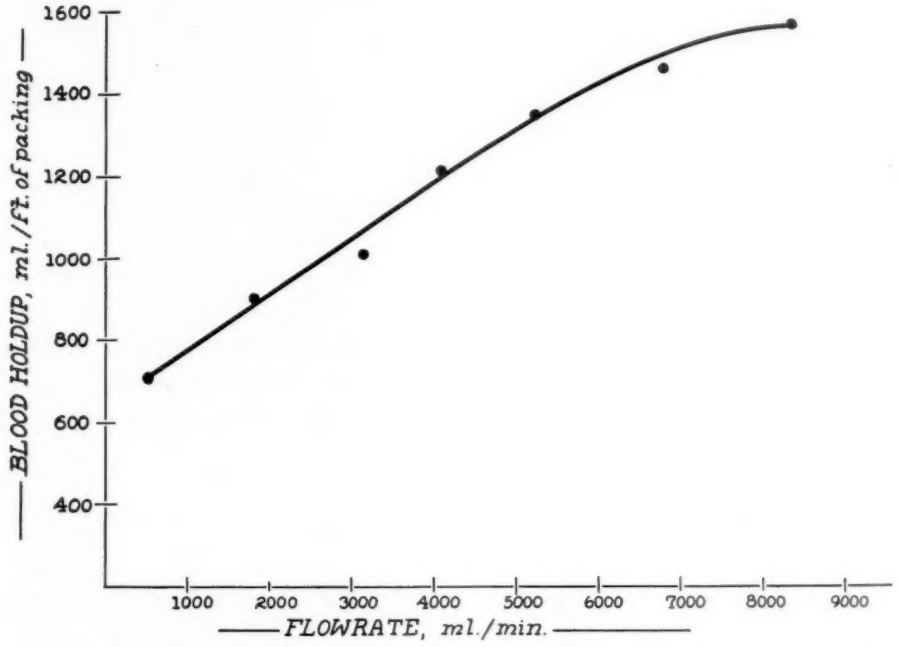

Fig. 9.—Stedman packing oxygenator: holdup as a function of blood flow.

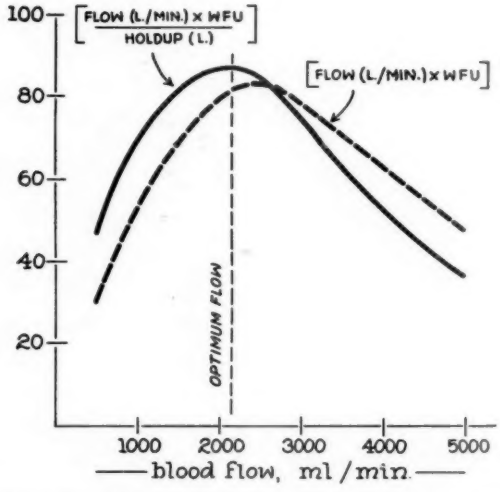

Fig. 10.—Stedman packing oxygenator: efficiency as related to blood flow.

the curve is extrapolated to zero flow, it becomes apparent that there is a holdup of about 600 ml. of blood per foot of packing that persists even at negligible flow.

Optimum blood flow: By multiplying the change in work function at a given flow, Fig. 8, by the flow itself and plotting the product against flow, we obtain the dotted curve of Fig. 10. This curve gives the number of work function units which are introduced for any given flow. The solid curve of Fig. 10 represents the work function units introduced, divided by the holdup. The flow at which the maximum of this curve appears represents the point of highest efficiency. This occurs at approximately 2,100 ml. per minute. Since this flow is distributed over a six-inch diameter circle, an area of twenty-eight square inches, the blood flow for peak efficiency should be 110 ml. per minute per square inch. (This is a useful design figure since Stedman packing is available in various diameters.)

Overpressure oxygenation: In Table IV, the results for two experiments performed at the same flow and column height but at different oxygen tensions are recorded. An appreciable gain in oxygenation is noted with the higher oxygen tension. This gain is compared to the ratio of the oxygen diffusion gradients (P_{O_2} in gas – average P_{O_2} in plasma).

TABLE IV. OVERPRESSURE OXYGENATION WITH STEDMAN PACKING

RUN NO.	BLOOD FLOW (ML./MIN.)	SATURATIONS (PER CENT) INITIAL	SATURATIONS (PER CENT) FINAL	DIFFERENCE IN WORK FUNCTION (wfu)	RATIO OF DIFFERENCE IN wfu	AVERAGE OXYGEN GRADIENT (MM. HG)	RATIO OF GRADIENT
D9	2,700	47	72	25.7	1.7	630	1.5
M2	2,700	35	78	43.1		940	

Efficiency: The comparative efficiency is $\frac{1.8 \text{ ml./min. (blood flow)}}{\text{ml. (holdup)}}$ when the oxygenator is operated at its most efficient flow.

THE FOAM OXYGENATOR

Description of Apparatus.—The foam oxygenator,[10] shown schematically in Fig. 11, consists of a two-inch diameter commercial Pyrex pipe* which has at its top a six-inch diameter bowl. At the bottom of the pipe there is an oxygen manifold consisting of 125 2½ inch long 25 gauge hypodermic needles. Blood is slowly admitted at the bottom of the column, and is permitted to rise above the tips of the needles. The oxygen passing through the needles bubbles through the blood, forming foam as it emerges from the blood. The foam continues to rise until the whole column above the blood is filled. When the foam contacts the Antifoam-coated vertical baffles in the bowl, it breaks, the gas from each bubble passing upward through the baffles and out of the oxygenator, and the blood surrounding each bubble trickling down through the column until it reaches the pool of blood at the bottom. Venous blood is now admitted through the showerhead distributor and cascades down through the

*Available from Sentinel Glass Company, Hatboro, Pa.

foam being oxygenated in the process. The arterialized blood is withdrawn from the bottom of the oxygenator. Three distinct gas-liquid phases are apparent when the oxygenator is in operation: 1. At the bottom there is a pool of blood through which bubbles are rising freely as they are emitted from the oxygen manifold. In order to prevent oxygen embolism, the bubbles must have a rate of ascent greater than the rate of descent of the blood being withdrawn from the oxygenator. The larger the bubble, the more rapidly it climbs. At low oxygen flows, the bubble size is determined largely by the size

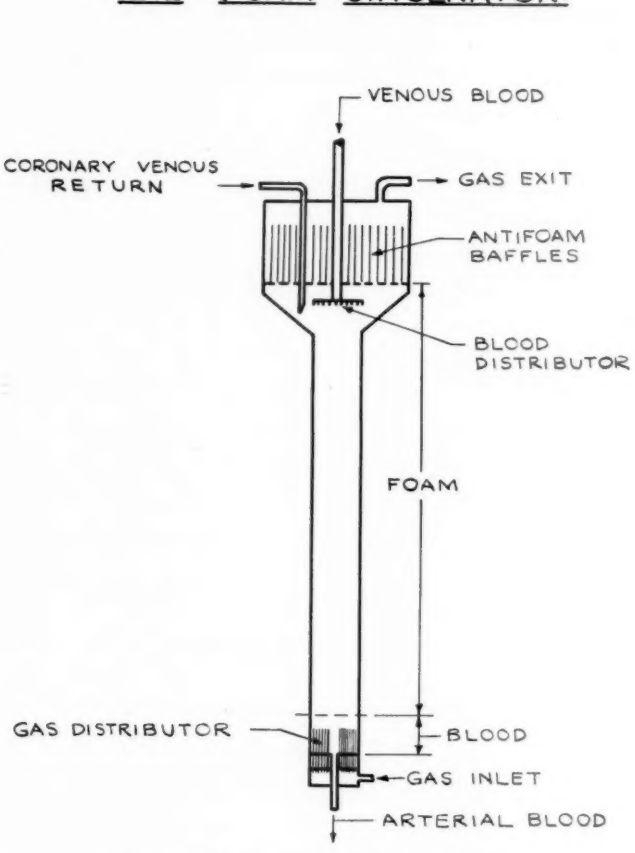

Fig. 11.—Foam oxygenator: schema.

of the orifice; the diameter of the bubble is proportional to the cube root of the diameter of the needle.[17] (Bubbles released from coarse sintered glass disks are not consistently large enough to avoid gas embolism under normal operating conditions.) 2. Above the blood pool there is a foam column where the bubbles are separated by rather heavy blood films. 3. The bubbles above the blood distributor are bound by thin blood films since only the blood released by the defoaming baffle passes down through them.

The maximum gas flow which can be passed through the oxygenator is determined by the capacity of the defoaming system. A defoaming baffle

consisting of one-quarter inch diameter plastic tubes cut into three-inch lengths coated with Antifoam and packed vertically into the defoaming bowl is capable of defoaming a gas flow of 6.5 ml. per minute per square centimeter of defoamer cross section with dog blood. Another type of stationary baffle is formed by a three-inch-wide stainless steel sheet wound into a helix with one-eighth inch spacing between the turns. In the large bubble oxygenator of Thomas, defoaming is accomplished by pulsatile, high-velocity jets of air which mechanically break up the foam. This system has the advantage over the stationary defoamers described in that no antifoam compound need be used.

Practical Operation.—When this oxygenator is used in a perfusion circuit, the arterial pump is continuously adjusted to maintain the blood-foam interface about two inches from the bottom of the column. At the site at which the interface is to be observed, the glass should not be siliconed, or else static bubbles will adhere and obscure the view.

To obviate channeling, the oxygenator should be aligned vertically.

If the oxygenator is not used at atmospheric pressure, a large flow resistance placed between the oxygen tank and the oxygen manifold will reduce fluctuations in the gas flow due to fluctuations in the pressure within the oxygenator. We have used a filtration candle* submerged in water for this purpose. To gauge the gas flow it is desirable to use a flowmeter.†

Results.—In contrast to film oxygenators, the operation of the foam oxygenator is greatly affected by the magnitude of the gas flow. This additional variable makes the specification of the conditions for its operation more complex.

Gas flow: The gas flow which combines optimum oxygenation with a low holdup is of the order of 70 ml. per minute per square centimeter of cross-sectional area. At higher flows there is a steep increase in holdup, while at lower flows the oxygenator eliminates less carbon dioxide.

To eliminate the CO_2 production of a twenty kilogram dog, a gas flow of about 140 c.c. per minute per square centimeter is needed. At lower flows the tendency toward respiratory acidosis is self-limiting, however, since the higher the CO_2 tension of the blood, the more CO_2 any given volume of oxygen will be able to carry away.

Blood flow: The blood flow through the column should not exceed 140 ml. per minute per square centimeter if an orderly foam column is to be maintained. At higher flows the blood-foam interface becomes difficult to distinguish.

Work function: The work function for the foam oxygenator is shown in Fig. 13. It differs from the work function of the Stedman packing and spinning disk oxygenators in that it falls off less rapidly at higher saturations.

Oxygenating characteristics: With the blood flow and gas flow as given previously, this oxygenator will introduce a work function difference of 1.8 wfu per inch of column height for blood of 15 Gm. per cent hemoglobin.

*No. 03 filter candle, Selas Company, Philadelphia, Pa.
†Rotameter type instrument, Fisher and Porter Co., Hatboro, Pa.

Design procedure: Suppose one wants a foam oxygenator which will oxygenate a maximum blood flow of 4,000 ml. per minute from 60 per cent to 90 per cent. The work function difference from 60 per cent to 90 per cent is found from Fig. 13 to be 100 – 60 = 40 wfu. The height of the oxygenator therefore should be $\frac{40}{1.8} = 22$ inches. The cross-sectional area of the oxygenator is found to be $\frac{4{,}000}{140} = 28.5$ cm.^{2} This is equivalent to a 2.4 inch diameter tube. The gas flow is $70 \times 28.5 = 2{,}000$ c.c. per minute.

Holdup: The holdup for beef blood having a concentration of 12 Gm. per cent hemoglobin at 37° C. is given as a function of blood flow in Fig. 12. The holdup is expressed as the fraction of the total oxygenator volume which is occupied by the blood. The holdup for undiluted blood may be expected to be somewhat higher than that shown in Fig. 12 because of the increased viscosity.

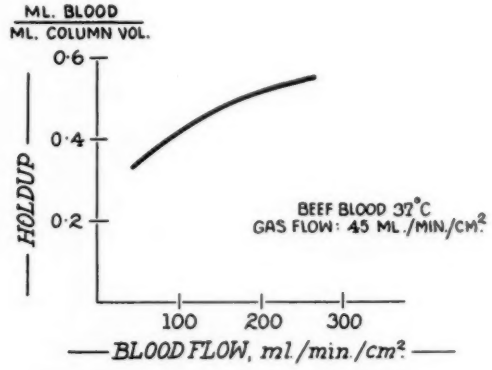

Fig. 12.—Foam oxygenator: holdup.

Efficiency: The efficiency of the foam oxygenator for a gas flow of 70 ml. per minute per square centimeter and a blood flow of 140 ml. per minute per square centimeter is $\frac{4.0 \text{ ml. (blood flow)}}{\text{ml. (holdup)}}$.

Bubble size: In order to determine the bubble sizes for maximum efficiency, experiments were carried out with oxygen manifolds consisting of Nos. 17, 21, 22, 23, and 25 hypodermic needles.

The number of needles in each manifold was chosen so that the total cross-sectional area of the needles was the same in each manifold. Since bigger needles produce bigger bubbles and since the ratio of surface area to volume decreases with increasing bubble size, one would expect a lower efficiency with the bigger needles. The holdup, however, is less for larger bubbles. The combined effect of these two opposing tendencies was found to be a drop in efficiency for the larger bubbles. Thus, the efficiency for the Nos. 21, 22, and 23 needles was 20 per cent lower than that for the No. 25 needles. The possibility remains that the greater ease of defoaming large bubbles may indicate

the use of the larger needle sizes despite their drop in efficiency. The use of needles smaller than No. 25 (.010 inch internal diameter) would be more efficient but raises additional problems. The needles are difficult to handle and to clean, defoaming becomes more difficult, and embolism is a possibility.

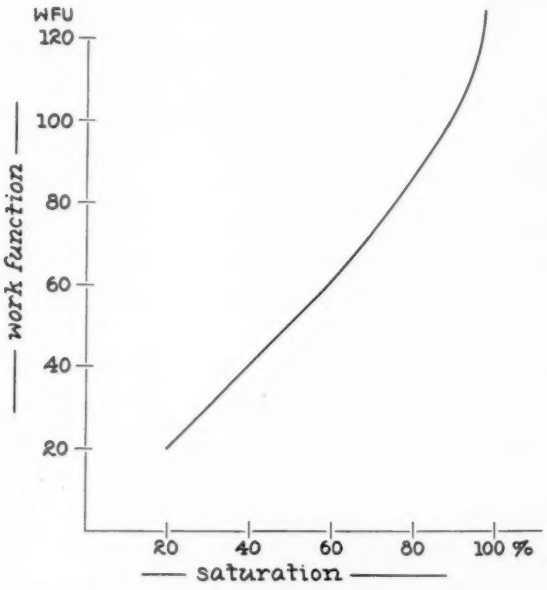

Fig. 13.—Foam oxygenator: work function curve.

SUMMARY AND CONCLUSIONS

1. The major physical problem for artificial oxygenators is the rapid introduction of oxygen into the plasma. A high oxygen diffusion gradient and a high degree of turbulence in the blood are the principal means of expediting oxygen transfer.

2. Oxygenators expose individual blood films for periods of time without regard to the degree of hemoglobin unsaturation. Thus, this time is used less efficiently at high saturations since the surface blood is saturated before the termination of the exposure time. Thus, more oxygenator working space and time are required to increase the hemoglobin saturation from 80 to 100 per cent than from 60 to 80 per cent. As a means of quantitating the relative difficulty in oxygenating over various saturation ranges the work function is introduced.

3. To increase the precision of the concept of oxygenator efficiency, it appears desirable to compare oxygenators working within the same saturation range, and that of 60 to 90 per cent is arbitrarily chosen. We therefore define comparative efficiency as follows: The largest flow of blood of 15 Gm. per cent hemoglobin which the oxygenator can raise from 60 to 90 per cent saturation divided by the total blood holdup at this flow rate.

4. Some experimental techniques of evaluating oxygenators through in vitro studies are outlined. The power to control and stabilize blood flow and

oxygen saturation is of great value in obtaining results for comparison of apparatus.

5. The efficiency of the spinning disk oxygenator varies directly with minute exposure area. Larger disk area and greater speed of rotation increase oxygenation linearly. With disks of 19.7 cm. diameter, foaming renders operation at over 105 r.p.m. impractical.

6. The Stedman packing oxygenator operates with a peak efficiency at a blood flow of about 2,100 ml. per six-inch diameter circle.

7. The efficiency of both spinning disk and Stedman packing oxygenators is increased by 50 per cent when the oxygen diffusion gradient is increased by 50 per cent.

8. The foam oxygenator operates most efficiently with an oxygen flow of 70 ml. per minute and a blood flow of 140 ml. per minute per square centimeter. Larger bubbles decrease oxygenating efficiency by almost 20 per cent, but are more readily defoamed.

9. The comparative efficiencies of the three oxygenators studied are as follows: spinning disk, 1.7, Stedman packing, 1.8, foam, 4.0.

Acknowledgments.—The spinning disk oxygenator used in this study was generously made for us by the General Precision Laboratories, Pleasantville, N. Y., through the offices of Mr. Ivan Greenwood. The Stedman packing oxygenator was loaned to us by Dr. L. B. Bragg of the Packed Column Corporation, New York, and by Dr. John Gibbon. The Sentinel Glass Company, Hatboro, Pa., gave material assistance in the formation of the foam oxygenator. Polyethylene used for the defoaming baffle in the foam oxygenator was donated by Mr. Peter Seckel of the Anchor Plastic Company, New York. Polyvinyl tubing was generously supplied by the Sunlite Manufacturing Company, Milwaukee, Wis. Needle tubing was obtained through the kindness of Mr. Oscar Schwidetzky, Becton, Dickinson and Company, Rutherford, N. J. The blood pump used in many in vitro experiments is made by the Vanton Corporation, New York, and was generously supplied by Mr. J. J. Ashton and Mr. Gerald Lewis of that organization.

We are greatly indebted to many workers in the field of mechanical pump-oxygenators who advised us, showed us the detailed operation of their laboratories, and saved us from many futilities. We are especially obliged to Dr. John Gibbon and Dr. Bernard Miller, of the Jefferson Medical College, to Dr. Clarence Dennis and Dr. Dwight Spreng, of the New York State Medical College, to Dr. Leland Clark, Jr., and Dr. Frank Gollan of Antioch College, and to Dr. W. J. Kolff and Dr. Frederick Olmsted, of the Cleveland Clinic Research Institute. We are deeply indebted to Dr. David L. Drabkin and Dr. Edward Gordy for having introduced to us their method for the spectrophotometric determination of oxyhemoglobin. We wish to thank Dr. Harry M. Vars and Dr. James M. Walker of the Harrison Department of Surgcal Research for much advice and assistance.

We thank Miss Betsy Hoffer and Miss Florence Conway for the secretarial assistance which we received from them, and finally we wish to express our indebtedness to our technician Mrs. Frances Philips for her selfless and devoted contributions to our project.

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Book Reviews

Surgery for Nurses. By James Moroney, M.B., Ch.B., F.R.C.S. (Eng.), L.R.C.P. (Lond.), with a Foreword by Miss Dorothy M. Smith, O.B.E., Chairman of General Nursing Council for England and Wales, Matron, Guy's Hospital, London. Ed. 2. Edinburgh and London, 1952, E. & S. Livingstone. $6.00.

A surgical textbook of nursing, in order to achieve wide utility, must provide in a single treatise a broad discussion of all of the surgical specialties and the nursing requirements related to them. Despite the inherent disadvantages which this prerequisite creates, the author here has done admirably well.

As an introduction, the nurse is reminded of her increased responsibilities and the contributions, especially to surgical diagnosis, which are accomplished by her careful observation of the patient. There follows a detailed discussion of the fundamentals of preoperative and postoperative care, of the principles of surgical bacteriology and immunology, a description of the basis of inflammation, and a chapter on observations related to hemorrhage. These discussions on the principles of surgery are well done and are complemented by an adequate review of antibiotic therapy and an excellent description of surgical dressing techniques.

The clinical discussions of the General and Thoracic Surgery entities are quite adequate, as are those of the other surgical specialties, which include Urology, Neurosurgery, Fractures and Orthopedics, Otolaryngology, Ophthalmology, and Gynecology. There is besides this a brief "Introduction to Obstetrics." The correlation of the basic nursing functions and problems with these didactic clinical descriptions is an outstanding feature of the book.

There are certain differences from American textbooks which this book of English origin preserves. For example, there is a chapter devoted to the surgical forms of tuberculosis and a brief, but excellent, summary of the chemotherapy of tuberculosis. Such a presentation is probably uncommon in similar American textbooks.

On the other hand, some methods of surgical therapy are recommended or emphasized which are not largely acceptable in this country; they include a wider use of radiotherapy for malignant tumors of the head and neck, and an apparent enthusiasm for colonic restoration of the stomach following gastrectomy. There is a notable failure to emphasize the significance of nodular goiter as a precursor of carcinoma of the thyroid. These differences are not crucial and do not significantly influence the utility which the book is designed to have.

This is a well-recommended textbook for nurses.

Physiological Foundations of Neurology and Psychiatry. By Ernst Gellhorn, M.D., Ph.D., Pp. 556. Minneapolis, 1953, University of Minnesota Press.

In this volume Dr. Gellhorn has summarized over 100 of his own previously published investigations, as well as a large amount of other related work. The aim of the book, as stated in the preface, is more modest than the title implies. "By no means all, but only some, physiological foundations of neuropsychiatry are treated, those with which the writer is familiar through his own experimental work . . . it is hoped that significant topics have been selected, of interest to physiologists, endocrinologists, internists, neurologists and neurosurgeons, psychiatrists and students of human behavior."

After a review of current knowledge about neuronal activity, the motor cortex, and the physiology of movements, there is an outline of the physiologic basis of consciousness, in

which the author takes the position that "understanding the mind from the point of view of neurophysiology is not an entirely hopeless task." Then there is a discussion of autonomic functions, with an interesting chapter on the eye as an indicator of autonomic activity.

The section on "Integrations" includes chapters on the principles of neuroendocrine action, on the physiologic basis of emotion, and on homeostasis.

In the concluding section, entitled "Applications," one of the important topics discussed is the relation of mental processes to the central autonomic balance, and the use of autonomic tests in the analysis of psychoses. The effectiveness of shock therapy is shown to be related to increased and prolonged reactivity of the sympathetic hypothalamic centers.

The discussions of the topics chosen are lucid and thorough, and reveal the extensive experience and authority of the author.

Grenzen des Normalen und Anfänge des Pathologische im Röntgenbilde des Skelettes. By Dr. A. Köhler. Ed. 9. Pp. 672, with 1,282 illustrations. Stuttgart, 1953, Georg Thieme Verlag, Agent for U.S.A.: Grune & Stratton, Inc., New York, N. Y.

The boundaries between the normal, the anomalous, and the pathologic remain poorly defined. This is especially true of the anatomy of the skeleton as displayed on roentgenographs. Köhler published this monograph as a guide for use in interpreting x-ray photographs which were not entirely normal or obviously pathologic. The ninth edition is as valuable today as was the first edition in 1910. The normal variations and anomalies of the skeleton are catalogued in a systematized manner well designed for easy reference. In addition to reproductions of typical examples, there are comprehensive charts and drawings which summarize this information. A large number of examples of various disease processes of bone in their earliest stages are inserted throughout to aid in differential diagnosis. The bibliography has been brought up to date and includes a large number of references from the recent European medical literature. This is a necessary reference book for roentgenologists, orthopedists, and fracture surgeons. It is not necessary to have a fluent reading knowledge of German to utilize the information presented. The publishers have used good paper, and the illustrations are clear and well chosen.

ANNOUNCEMENTS

Third International Congress on Diseases of the Chest

The Third International Congress on Diseases of the Chest, sponsored by the American College of Chest Physicians every second year, will be held in Barcelona (Spain) Oct. 4-8, 1954.

Communications will be held on diseases of the chest and thoracic surgery, including anesthesiology, experimentation, tuberculosis, cancer, thoracic wall, lung, pleura, mediastinum, esophagus, pericardium, heart, great vessels, and diaphragm.

During the celebration of the Congress, an exposition of surgical, clinical, radiologic, and photographic materials, as well as pharmaceutic products, books, and arts related to medicine, will be held at the Hospital de la Santa Cruz y de San Pablo of Barcelona, meeting place of the Congress.

All physicians and surgeons who wish to attend the Congress should write for application and any other information to Dr. A. Caralps, General Secretary of the Congress, Córcega, 393, 4.°, 1.ª, Barcelona (Spain).

Sixth Congress of the Pan-Pacific Surgical Association

The Sixth Congress of the Pan-Pacific Surgical Association will be held in Honolulu, Hawaii, Oct. 7-18, 1954. Doctors are cordially invited to attend and are urged to make arrangements as soon as possible if they wish to be assured of adequate facilities.

An outstanding scientific program with over 100 leading surgeons, including sessions in all divisions of surgery and related fields, promises to be of interest to all members of the profession.

The Association office has been appointed as travel agent for those attending the Congress and it is important that all hotel and travel reservations be made through the Honolulu headquarters of the Pan-Pacific Surgical Association.

For further information, write to F. J. Pinkerton, M.D., Director General, Pan-Pacific Surgical Association, Suite Seven, Young Building, Honolulu, Hawaii.

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